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## LYMPHOGENOUS INFECTION OF THE CENTRAL NERVOUS SYSTEM.

BY DAVID ORR, M.D.
*County Asylum, Prestwich*
AND
R. G. ROWS, M.D.
*County Asylum, Lancaster.*

The obscurity which surrounds the genesis of almost all inflammatory lesions in the central nervous system, and of those which are degenerative except where a focal lesion exists, will be admitted. The questions of the causation of the lesion, the point of origin of the morbid change and its propagation, are constantly recurring in regard to cases of meningitis, myelitis, tabes dorsalis, dementia paralytica, and the non-systemic scleroses, and the theories advanced have often been based on assumptions devoid of proof which have tended rather to divert the investigator from, than to lead him on to, the right path. Nor should one be astonished that this is so, for the intricate anatomy of the nervous system, its complexity of function, and its comparative inaccessibility to experimental methods, have taxed the ingenuity of the investigator to the utmost. Hence the theories regarding the genesis of many morbid phenomena have been based upon deductions built up on the examination of tissue in which the chronicity of the changes obscured the original starting-point of the retrograde or inflammatory process. This applies particularly to subacute and chronic lesions, systemic and non-systemic, affecting the columns of the spinal cord.

For years it has been apparent that continued examination of these chronic lesions while increasing our knowledge in detail yet failed to widen it in regard to etiology, and though toxic influence naturally received due recognition, its source and mechanism of action remained

unexplained. It seemed obvious, therefore, that investigation ought to be directed towards elucidating the mechanism of production of those lesions and the first step naturally involved a study of all possible paths of infection and intoxication. It is with one of these, infection via the lymphatic system of peripheral nerves, that this paper mainly deals; and in it we propose to give a synopsis of our observations in clinical cases and experiment. Much of the detail on which our conclusions have been founded must necessarily be omitted; that will be found in the appended list of publications.

In all probability the controversy surrounding the genesis of the lesion in tabes dorsalis and the recognition of dementia paralytica as an inflammatory disease were most important factors in directing attention to the lymphatic system of the cerebrospinal axis; and an important step forwards was taken with the demonstration of a continuity of the lymph-stream in peripheral nerves with that of the spinal cord. The injection into nerves of organisms and coloured substances showed that the lymph-stream was an ascending one towards the cord and that the main current lay at the periphery of the nerve-bundles immediately under the fibrous sheath. It must be borne in mind, however, that this statement regarding the main current of lymph in nerves was based on experiments in which organisms have been injected into the nerve substance. Where infection occurs from without it will be shown that diffusion of organisms and toxins can take place along the outer surface of nerves and give rise to an ascending epi- and perineuritis.

Infection along peripheral nerves had been deduced for many years in regard to tetanus and rabies, and the recognition of a wider application of this principle suggested a new line of research along which an explanation of certain other pathological phenomena might be sought. Valid proof of the principle will be found in the following short résumé of the literature.

Marie and Morax [18] cut the nerve to the fore limb of an animal, and later injected a lethal dose of tetanus toxin into its paw with a negative result. Homén and Laitinen [13] injecting streptococci into the sciatic nerve, traced them upwards into the meninges of the cord; while Pirrone [34], employing the pneumococcus, found changes in the cord limited to the side corresponding to the infected nerve. In addition to organisms, chemical and inert substances yielded equally instructive results. Guillain [12] injected ferric chloride into the sciatic nerve, and subsequently introducing potassium ferrocyanide into

the general circulation found Prussian blue in the posterior roots; he also found that coloured fluids diffused from the pial lymph spaces of the posterior part of the cord into those of the posterior columns. Marie and Guillain [19] concluded from their work that there is a common lymph system for the posterior roots, the posterior columns and the pia covering them, and that the lymph flows freely in the intervals between the fibres and other structures. They state that tabes is a lesion of this system, most probably of syphilitic origin. Sicard and Bauer [39] injected china ink into nerves and found that the granules ascended along them to the cord; and according to D'Abundo [2] and Guillain [12] the lymph in the posterior columns pursues an ascending course and simultaneously passes forwards towards the central canal. In these experiments therefore we are afforded ample evidence of the possibility of lymphogenous infection of the central nervous system.

Homén's [13] investigations are particularly convincing. Twenty-four hours after the injection of bacteria into the sciatic nerve, they accumulate in the lymphatic space situated on the internal surface of the perineurium and can be traced along the internal surface of the capsule of the spinal ganglion, along the inner surface of the perineurium of the spinal roots, especially the posterior, and into the cord meninges, from which they spread into the peripheral zone of the cord and especially along the postero-median septum. The bacterial invasion is accompanied by inflammatory reaction, which on experimenting with pure toxin is of less degree and inconstant.

Spitzer's [40] experiments, too, are extremely interesting. He injected an infusion of jequirity (*Abrus precatorius*) into the dental pulp of a dog and killed it after some days. Microscopic examination revealed an ascending inflammatory neuritis spreading up to and implicating the Gasserian ganglion. Zalla [44], in whose monograph there is an excellent review of the observations on ascending neuritis, has employed the same methods of experiment as Spitzer [40] and Homén [13]. He has not confirmed the former's work but acknowledges the great importance of Homén and Laitinen's [13] researches. Zalla [44], employing the *Bacillus pyocyaneus*, demonstrated acute inflammatory phenomena, spreading up the sciatic nerve through the spinal ganglia and spinal roots, especially the posterior, into the cord and meninges. After careful criticism he agrees that Homén's [13] conclusions are correct and admits the possibility of the diffusion of an inflammatory process along peripheral nerves to the central nervous system by experiment. While admitting this

experimental diffusion he is careful at the same time to point out that it differs greatly, in its course, from the true ascending neuritis found in the human subject. This point, however, need not be considered at the present moment; it is of minor importance as compared with the fact that organisms and toxins can reach the central nervous system by diffusion along the lymph path of peripheral nerves.

Evidence of Infection of the Central Nervous System by Toxic Diffusion along the Perineural Lymph System in Clinical Cases (Lymphogenous Infection).

In 1903 we had the opportunity of examining the nerve tissues in a case of left brachial neuritis of twelve days' duration. The exciting agent in this instance was the *Staphylococcus pyogenes aureus*. We found the brachial plexus bathed in pus which had burrowed among the cervical muscles as well and surrounded the root ganglia of the cervical cord. The microscopic examination of the tissues proved of great interest. The loose areolar tissue round the spinal root ganglia of the left side was greatly inflamed, the veins were thrombosed and contained many cocci. Those not thrombosed were greatly congested; the arterioles, on the other hand, showed no morbid change. In the ganglion capsule there were hæmorrhages and cocci, more evident in the outer layers, and amongst the nerve-cells dilated venules and capillaries containing micro-organisms. Similar changes affected the perineurium of the brachial plexus, but to a less degree. No cocci were found in the dura of the cervical cord or loose areolar tissue covering it. One small group only was observed in the pia-arachnoid covering the posterior columns. There were no inflammatory phenomena in either membrane. The 6th and 8th cervical root ganglia of the right side were examined. There were no thrombi in the capsular areolar tissue, but scattered hæmorrhages in which were a few cocci. No cocci were found in the ganglion substance.

The extramedullary portion of the anterior and posterior cervical roots was examined for degeneration by Marchi's method and none was found. In the spinal cord, however, the same method demonstrated an acute degeneration whose distribution was confined to the cervical region. The seventh, sixth, and fifth segments showed much the greatest degree of degeneration. There was marked degeneration of the intramedullary portion of the left posterior root, which, commencing at the point where the fibres lose their neurilemma sheath, affected the middle area of the root entry zone. On the right

side the degeneration affected the same area, but was less marked. There were degenerated fibres on each side of the postero-median septum. In the lateral columns of the cord on either side of the septa derived from the pia-arachnoid there was a considerable degree of myelin degeneration; and here and there in the posterior and lateral regions there were degenerated myelin droplets at the cord margin. A considerable degree of degeneration was observed in connection with the intramedullary portion of the anterior roots in their whole course from the cord periphery to the grey matter. There was degeneration of the collaterals running from the left root entry zone to the anterior cornual cells, and also of the anterior commissure. All the vessels of the cord and meninges were greatly congested.

Special attention should be directed to one point in this case, and that is the presence of a gross degenerative lesion in the spinal cord of purely toxic origin. The toxins must have passed along the perineural lymphatics from the infective area round the spinal ganglia and brachial plexus; once having gained the cord they flowed with the lymph into the anterior and posterior root entry zones, and also round the cord in the meshes of the pia. When we come later to study the inflammatory lesions induced by infecting the lymphatic system of nerves it will be seen that precisely the same situations are involved.

Further evidence will now be brought forward in the following series of cases in support of the view that lesions of the spinal cord can result from the diffusion of toxins upwards along nerves from peripheral foci of infection. The description of the cases is condensed in order to save useless repetition.

*Case* 1.—Bedsores: gluteal region, more severe on left side: suppuration of right elbow.

Degeneration of the posterior columns and of the anterior radicular fibres in the lumbo-sacral region from S1—L3, more intense on the left side and in L4. From D12—D2 there was nothing worthy of note. Degeneration again commenced at D1 in the root entry zone of the right side: the lesion was most marked in C7 and C6, and gradually diminished in the next few segments.

*Case* 2.—Bedsores on buttocks and sacrum: of longer duration on the right side.

Lesion most intense on the right side. Slight degeneration of posterior columns in S1; maximum in L4 and 3: diminished gradually in the segments above this level.

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| *Case* 3.—Pelvic cellulitis, renal abscesses, double empyema of longer duration on the left side, abscesses in the cervical muscles. | Very slight degeneration of the posterior columns in the sacral region. Much Marchi reaction among the anterior radicular fibres of S4—3—2, especially on the left side. No changes in the lumbar cord. Degeneration in the root entry zones of D11—10—9; again a separate lesion beginning in the root entry zone of D5, more marked on the left side, and occurring in every segment as high as C4. In the cervical region the degeneration was greatest in C7 and 6. |
| *Case* 4.—Caries of the 4th and 5th lumbar vertebræ; psoas abscess on the right side, which became septic two months before death. | In S2 a slight lesion of the posterior columns, which increased in S1, and was most intense is L4 and 5. Above this level it gradually diminished. The lesion was much more marked on the right side. |
| *Case* 5.—Chronic suppuration of right knee-joint. | Degeneration of the posterior columns from S1 to the lower dorsal region, most marked on the right side and in L4—3—2. |
| *Case* 6.—Chronic suppuration of left knee-joint. | Lesion of the posterior columns most intense on the left side: slight in S1, well marked in L5—4—3. The lesion ceased at D11. |
| *Case* 7.—Prostatic cancer; chronic cystitis. | Followed by transverse myelitis at level of D8 and 9. |

All the above cases were studied by the Marchi method for myelin degeneration, and all showed involvement of the posterior columns in that region of the cord which corresponded to the nerve supply of the infective focus. At times also the anterior radicular fibres were affected. Case 1 and the case of brachial neuritis illustrate these two points very well. Another noteworthy point is that the degeneration of both anterior and posterior spinal roots always begins at the point where the fibres entering the cord lose their neurilemma sheath, that is in the intramedullary portion, and in the case of the anterior roots the degeneration in some instances has been traced from the cord margin into the grey matter, where it terminated among the cells. The effect of the toxins is not always exerted on the lateral portions of the cord. In the case of brachial neuritis, however, we find the lateral

diffusion very marked, a fact to be explained in all probability by the high activity of the infective focus and its close proximity to the spinal cord. The greater the degree of toxicity, therefore, in the lymph-stream, the more diffuse the cord lesion.

The extramedullary portions of the spinal roots in the above cases were examined for degeneration with a negative result. It seems clear, therefore, that toxins can ascend along the perineural lymphatics without producing parenchymatous changes in the nerves. On reaching the cord, however, they give rise to a degeneration of the myelin sheaths with which they come into contact. At the same time, in saying this we do not mean to affirm that parenchymatous changes are absent in all cases. It will be shown in another part of this paper how organisms and toxins cause an epi- and perineuritis as they pass upwards along the nerves; and it is conceivable that such, if of an acute nature or in action for a prolonged period, would tend to induce secondary parenchymatous changes, especially were an extension of the inflammatory process to take place along the septa between the nerve-bundles.

### Evidence of Lymphogenous Infection of the Central Nervous System from Experiment: Degenerative Lesions.

When the examination of clinical material had shown that lesions in the central nervous system had a definite anatomical relationship with the nerve supply of peripheral infective areas, and that these lesions depended upon toxic diffusion along the perineural lymphatics, it seemed that to submit this view to experiment would be the most certain method of obtaining definite data.

Instead of injecting organisms or toxins into the nerves on which it was proposed to operate, we placed a celloidin capsule containing a broth culture of a micro-organism in contact with the nerve. In one series of experiments this was placed under the gluteal muscles alongside the sciatic nerve; in another series under the skin of the cheek. The animals experimented upon were rabbits and dogs, and the organisms used were *Staphylococcus pyogenes aureus*, *Bacillus pyocyaneus*, Gaertner's bacillus, *B. coli*, *B. botulinus*, and a culture of a diphtheroid bacillus obtained from a case of dementia paralytica. We commenced experimenting with all these bacilli, but later adopted a strain of *S. aureus* whose virulence had been raised. It was also found expedient to renew the capsule at intervals. Some of these capsules remained intact, others did not, and a variable amount of leakage occurred. The tissues from the first series of experiments were prepared for examination

of the degenerative changes in the medullated fibres of the nerves, cord, medulla, and pons. Marchi's osmic acid method was employed. Those from the next two series were prepared to demonstrate the inflammatory phenomena. The capsules were left *in situ* for periods of from fourteen days to six weeks. Control experiments were carried out with capsules containing sterile broth.

### Capsule in Contact with Sciatic Nerve.

In the lowest segments of the cord no degeneration was found. Marchi's method, however, gave a positive reaction in the lumbar enlargement. The degeneration of the exogenous system of the posterior columns was seen to begin immediately at the point where the fibres lose their neurilemma sheath; it involved the root entry zone and the remainder of the columns with the exception of a small area behind the commissure and the posterior periphery of the cord. There was considerable degeneration of the collaterals, which principally affected those running through the antero-internal angle of Rolando's substance in the posterior grey horn; those passing towards the anterior cornua showed much less alteration. The degeneration diminished rapidly in the lower dorsal segments.

In one experiment a capsule was also placed under the muscles of the upper dorsal region. The capsule ruptured and at *post-mortem* pus was found among the cervical muscles of the right side. There was degeneration of the posterior columns in the lumbar enlargement, distributed as noted above, which steadily decreased from below upwards, and in the lower dorsal cord consisted in a few scattered fibres round the postero-median septum. In the upper dorsal region considerable degeneration again appeared in the root entry zones, especially of the right side: this, however, was not so systemic in character as that of the lumbar region. In the cervical cord there was a marked increase in the number of degenerated fibres which filled the posterior columns, with the exception of the zone immediately behind the commissure and that adjoining the cord periphery. The collaterals leaving the root entry zones were degenerated, but not further anterior than the level of the commissure.

In one case there was also degeneration of the lateral columns in the vicinity of the posterior horns. The extramedullary portion of the posterior roots was examined by Marchi's method: no degeneration was present.

CAPSULE UNDER SKIN OF CHEEK.

The medulla and pons were cut in serial section and the Marchi method demonstrated degeneration of the cranial nerves in their intramedullary course. The degree of degeneration varied in intensity as well as in type.

*Third nerve.*—There was a high degree of degeneration of the third nerve from its point of emergence back to the nucleus of origin, towards which the morbid change diminished in intensity. The degenerated myelin showed as long, thin, black threads arranged in parallel or sinuous rows and with moniliform swellings.

*Fourth nerve.*—There was less degeneration in this than in the third nerve. There were short sinuous black filaments at the point of emergence. The degenerative phenomena decreased rapidly from below upwards and were absent at the nucleus of origin.

*Fifth nerve.*—The morbid change in both sensory and motor portions was very marked. In the latter were short, thin, black filaments with moniliform swellings intermingled with swollen globules which could be traced into the principal nucleus of origin and for a short distance upwards along the mesencephalic root. In the former there was a higher degree of degeneration which could be traced for a variable distance in the descending root; in one case the degeneration extended down as far as the lower part of the medulla. The degeneration began at the point where the neurilemma sheath ceases to exist, was very profound especially at and immediately inside this point, and all the way down the root was identical with the appearances found in Wallerian degeneration.

*Sixth nerve.*—There was a greater degree of alteration in this nerve than in any of the others, and the morbid appearances were similar in character to those in the third nerve. The maximum of degeneration occurred in this nerve between a point just posterior to the corpus trapezoides and the margin of the pons. Here the myelin was fused into short and long masses of somewhat sinuous outline; some ended in swollen bulbs, others were prolonged into fine black threads. There were many scattered isolated threads and also polymorphic globules. In the middle third of the nerve were sinuous rows of fine black filaments running parallel to each other, and towards the nucleus of origin these filaments of degenerated myelin were finer, fewer in number and could be traced curving round the ascending portion of the seventh nerve to the floor of the fourth ventricle.

*Seventh nerve.*—The degeneration here was much less. It commenced at the point where the neurilemma left the nerve-fibre and decreased centralwards; near the nucleus there were merely traces of altered myelin. In the distal portion and ascending limb the degeneration was mostly of the fragmentary type mixed with a few black filiform varieties.

*Eighth nerve.*—The degree of degeneration was slight and only seen in the cochlear division where there were a few black threads with moniliform swellings ending abruptly lateral to the restiform body.

*Ninth, tenth, eleventh, and twelfth nerves.*—In these there were no changes worthy of note. The extramedullary portion of the cranial nerves was examined by Marchi's method and no degeneration was present. The degeneration in the pons and medulla was strictly confined to the intramedullary course of the nerves, except in one instance where there was some degeneration of the fibres of the corpus trapezoides on either side of the sixth nerve for a short distance.

The alteration in the myelin sheaths is rather unusual, especially that in the motor cranial nerves. In the sixth, for example, there were many grades of degeneration. In the initial stage the myelin stained darkly (Marchi method), was swollen and vacuolated, later it formed thick fusiform masses and then elongated moniliform structures. The distal segment of the intramedullary portion of the nerve suffers most, and presumably the morbid change spreads from the periphery to the nucleus of origin. With this there is no change in the extramedullary part, so that the degeneration is clearly not Wallerian. The mode of extension and the appearance of this variety of degeneration is typical of acute toxic infection and is known as "segmentary necrosis." The black fusiform masses and long sinuous threads indicate an acute necrotic or liquefactive change in the medullary sheath.

In all the other cranial nerves and in the spinal cord one can see abundant evidence of primary myelin degeneration of varying degree. At times the sheath showed degeneration in the neighbourhood of the axis cylinder, at others the periphery was affected. In the descending root of the fifth in the pons and medulla, and in the root entry zone and collaterals of the spinal cord the degeneration was typically Wallerian in character, the degenerate myelin fragments and globules lying in rows along the course of the nerve and reaching in the case of the fifth cranial nerve to the lower part of the medulla.

From the clinical cases and the results of experiments we arrive at the following conclusions: (1) In spinal and cranial nerves there is an

ascending lymph-stream to the central nervous system whose main current lies in the spaces of the perineural sheath. Toxins reach the spinal cord and brain by this route; and although they spread to some degree in the lymph-spaces of the pia-arachnoid, and so may affect structures at a distance from the point of entrance, they pass for the most part in the main stream along the nerve roots into the substance of the central nervous system. (2) Outside the central axis the nerves are possibly protected by the vital action of their neurilemma sheath; most probably, however, it is the peripheral situation of the lymph current which is the deciding factor.

The following case, of which we give an abstract, confirms many of the observations to which we have just drawn attention. It was one of general paralysis of the insane, and at the autopsy in addition to the usual morbid appearances there was acute hæmorrhagic ulceration of the colon, especially in the lower portion, and an acute cystitis. The urine was blood-stained and very offensive. There was in addition suppuration in the right knee-joint of two weeks' duration. Cultures were made of the cerebrospinal fluid in the lateral ventricle and from the lumbar region, which yielded an abundant growth of a bacillus, rod-shaped as a rule, but often long and thread-like. The right sciatic nerve was examined for organisms with negative result. They were found abundantly in the following regions, however: the internal layers of the perineural sheath of the posterior and anterior lumbar spinal roots, amongst the fibres of the posterior root entry zone, in the lymph-spaces of the pia-arachnoid round the cord margin, in its septa passing into the cord where they were most numerous at the periphery, in the intramedullary portion of the motor fibres, and in the central canal and its neighbourhood. In the spinal roots the organisms were observed passing inwards along the septa. There were many organisms within the adventitial lymph-spaces of both cord and roots, but none within the lumen of the vessels. The vessels were dilated, congested, and the adventitial space infiltrated with small round cells. The organisms within the cord, therefore, find their way into those areas which are affected in toxic diffusion. This is especially well brought out by reference to the case of brachial neuritis, in which it will be remembered the myelin degeneration was distributed in the posterior root entry zone, the anterior radicular zone, under the pia-arachnoid and along the septa to the central parts of the white matter.

This case of organismal infection is of considerable significance. It shows us that the cerebrospinal lymph flows into the adventitial

spaces of the vessels, which may thus be infected secondarily. We know, too, that the products of myelin degeneration in many cases may be swept into these spaces until the vessel stains jet black with osmic acid. It is most probable that the unity of the adventitial lymph system with the general lymph circulation in the cord is the true explanation of the vascular phenomena found in acute myelitic lesions, and that these should not be considered as of hæmatogenous but of lymphogenous origin. Strong support in favour of that view will be found in the next series of experiments.

### The Histological Evidence of Experimental Infection of the Central Nervous System by the Lymph System of Peripheral Nerves.

*Series* 1.—The method of experiment adopted was similar to that previously employed. The capsule containing a broth culture of an organism was placed under the gluteus maximus of a rabbit or dog and in contact with the sciatic nerve. The organisms employed for experiment were the *Staphylococcus pyogenes aureus*, a diphtheroid bacillus from a case of general paralysis of the insane, and the *Bacillus botulinus;* the animals were allowed to live for varying periods up to one month. At first we found that movements on the part of the animal caused the capsules to burst; this was reduced to a minimum by using small capsules and thus we obtained tissue free from suppuration.

After the tissue had been placed in formalin 10 per cent. for at least fourteen days, longitudinal sections were made of the trunk of the sciatic nerve in its whole length, and of the lumbo-sacral ganglia with the anterior and posterior roots attached. A portion of the celloidin capsule with the nerve adherent to it was embedded in paraffin, cut transversely, and the sections fixed on albuminized slides. We propose to begin our description with the morbid phenomena at this point and will then pass on to the changes in the epi- and perineurium, to the signs of irritation in the nerve, and finally, to those in the spinal roots and ganglia. The sections were stained either with toluidin blue alone, or counterstained with erythrosin.

#### *A.—Where no Suppuration occurred.*

In an experiment of ten days' duration, the inflammatory exudate binds the nerve fairly firmly to the capsule, and is composed of definite

layers (fig. 1). In that lying nearest to the capsule there are a large number of polymorphonuclear leucocytes mixed with many cells whose protoplasm is scanty in quantity and whose faintly stained oval nucleus of medium size contains very little chromatin (fig. 2). Many of these clear nuclei are considerably distorted, others are placed excentrically in a cell body of fair dimensions. Excentricity of the nucleus is frequently associated with diminution in size. The second layer is

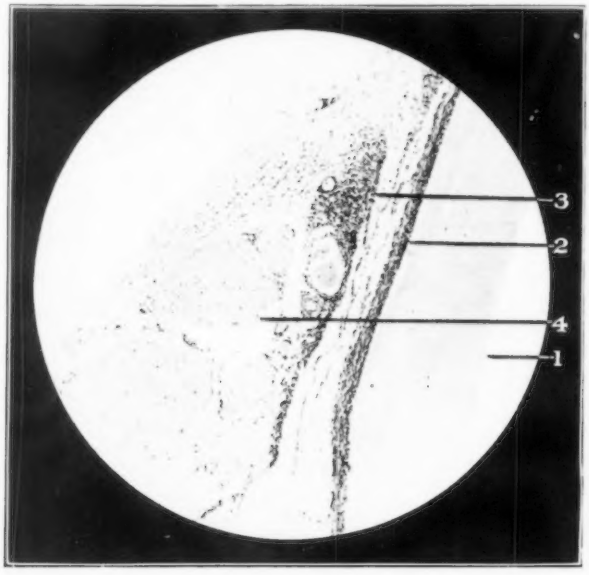


FIG. 1.—1, celloidin capsule; 2, layers of exudate; 3, granulation tissue in epineurium; 4, fasciculi of sciatic nerve.

composed almost exclusively of typical fibroblasts (fig. 2). Where it joins the first layer there are small round basophilic bodies suggestive of degenerated polymorphonuclear leucocytes; at its opposite margin are a few lymphocyte-like cells, some clear oval nuclei with little chromatin, and some young fibroblasts whose nuclei though elongated are still oval in contour. This fibroblast layer is intimately connected with the epineurium, which is intensely inflamed.

There is a change in the character of the cellular reaction immediately the line is crossed between the fibroblast layer and the highly

vascular epineurium. In this there are a large number of cells around the capillaries and veins; there are also groups of new vessels. With high magnification the adventitial sheath of the veins is seen to be infiltrated with small round cells whose nucleus stains deeply (fig. 3). Many of these surround the smallest vessels and lie free in the intervening tissue. In some, the protoplasmic body is indistinguishable; in many, however, there is a faintly stained narrow ring of cytoplasm; in others, again, the cell body is quite distinct, stains a violet colour,

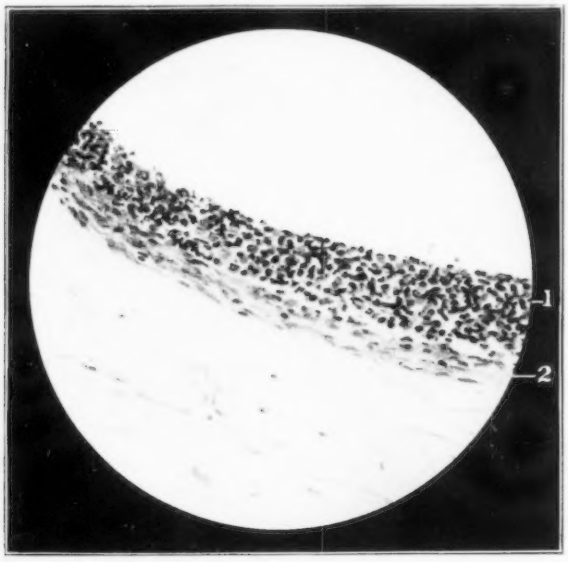


FIG. 2.—1, polymorphonuclear leucocytes mixed with large clear cells; 2, fibroblast layer.

and the nucleus is excentric. Around some capillaries and veins there are typical young plasma-cells with a round, excentric nucleus, a violet vaguely granular protoplasmic body, and a distinct crescentic halo at the central side of the nucleus (fig. 4). As we shall note the presence of plasma-cells frequently, it may be advisable to define what we mean by the term. The body, as a rule, is round, but may be fusiform or cubical according to pressure of numbers or the density of the tissue in which the cells are situated; the protoplasm stains of a blue or blue-violet colour, and we agree with Nissl [24] that while not definitely

granular, still it is not homogeneous. There is a halo of varying size at the central side of the excentric oval or round nucleus, in which strongly staining chromatin particles may be uniformly distributed, or arranged at intervals round the periphery—the "clock-face" appearance.

In the areas of new vessel formation there are many cells with a large clear oval nucleus scattered amongst the round cells. Sometimes no cytoplasm is visible; the majority, however, possess a small quantity

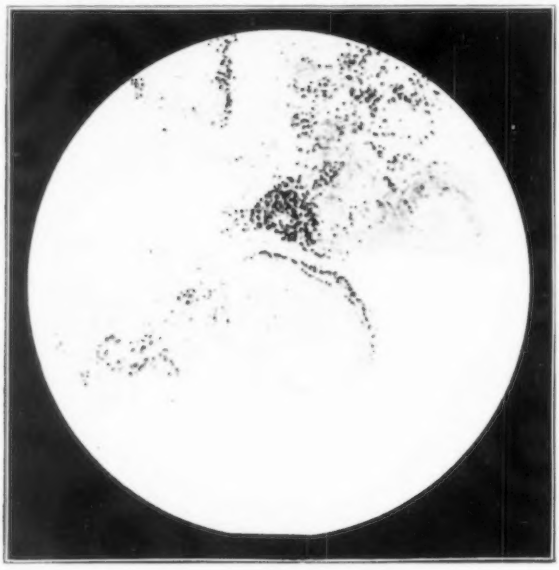

FIG. 3.—Small round-cell infiltration of epineurium and adventitial sheath of a vein.

of protoplasm which stains very lightly. In a limited number it is more evident and is drawn out at both ends of the cell as a fine thread, an appearance reminiscent of developing fibroblasts.

At the twentieth day much the same phenomena are seen, with, at the same time, some important though slight differences. In the polymorphonuclear layer next to the capsule the cytoplasm of the cells with clear oval nuclei is much more prominent. Some are reticular in appearance with a nucleus of irregular outline. In the second layer the transition from young to adult fibroblasts is very well seen, and is

indicated by the progressive flattening and elongation of the nucleus and by the marked increase in length of the protoplasmic body. On the side of this second layer which is nearest the nerve there are groups of reticulate cells, amongst which are a few fibroblasts. These cells possess a large, faintly stained reticular cytoplasm; in some the nucleus is large, pale, and irregular in outline, while in others it is much reduced in size, stains deeply, and is excentric in position.

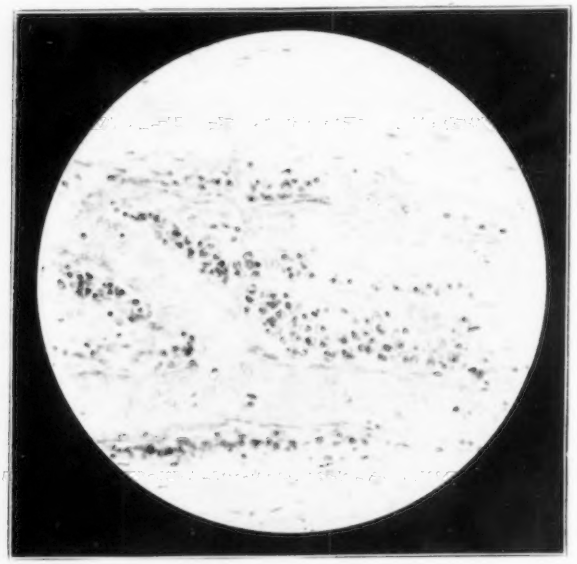

FIG. 4.—Plasma-cells round a vein. Note the absence of proliferation of the intima.

In some experiments the nerve was carefully stripped from the capsule and cut in longitudinal section in order to study specially the reaction phenomena in the epineurium. On the tenth day this highly vascular tissue shows a remarkable degree of inflammation, especially around the veins and capillaries (fig. 5). There are many proliferated nuclei, some of which are small, round, and deeply stained; others, again, are large and pale, with fine granules of chromatin. The majority of the pale nuclei are oval in shape and regular in outline; some, however, are more elongated or pear-shaped, and in others the nuclear membrane may be irregular or indented. The round, darkly stained nuclei occur

in large numbers, and there are plasma-cells in all stages of development amongst them. Many of these plasma-cells do not stain quite normally, and occasionally some are seen in a regressive phase in which the body is pale and hyaline, while the nucleus stains deeply and is crenated. The intima of the vessels around which this proliferation is occurring is comparatively free from irritative phenomena; all that is seen is swelling of the endothelial nuclei which may project into the lumen

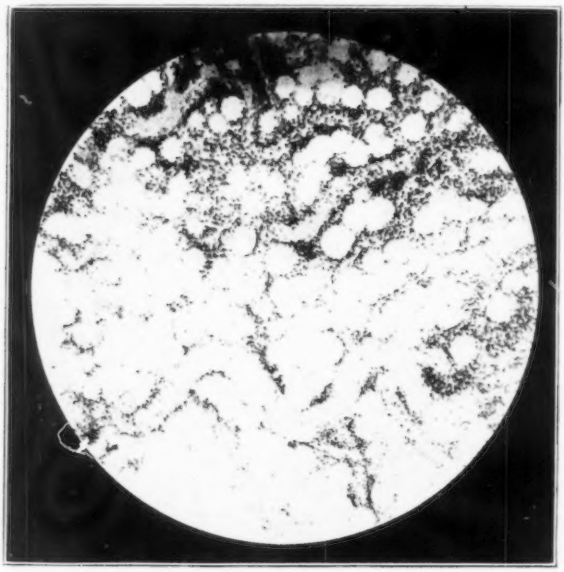

FIG. 5.—Proliferation of adventitia of veins in the epineurium.

or become detached. Occasionally, there are small collections of polymorphs and lymphocytes to be seen in the vessels and lying at the periphery of the blood-stream; this is the only evidence of participation of the hæmatogenous elements in the inflammatory process. The connective tissue nuclei of the areolar reticulum are pale, swollen and distorted, and there are plasma-cells lying, not only amongst them, but free in the spaces.

If the section happens to pass longitudinally through the adventitial coat alone a clearer estimate of the degree of proliferation in this sheath is obtained than if the lumen is included. The adventitial spaces are

filled with a mass of cells possessing large clear nuclei of almost every conceivable shape, and with plasma-cells in all stages of transition. In many of these the protoplasmic body is quite typical, but the nucleus, though excentric, is oval and clear and quite indistinguishable from a reacting adventitial nucleus. There are other plasma-cells of a more elongated type which somewhat resemble fibroblasts.

The degree of proliferative change in the perineurium is considerable. It is filled with clear nuclei of varying shape, round, oval, elongated and narrow, and irregular. The cell reaction is less in the inner layers. Amongst the proliferated nuclei are numerous plasma-cells, whose shape varies considerably, probably on account of the pressure exerted by this dense lamellar tissue. Many are triangular, others markedly elongated. All show the characteristic vaguely granular body with the halo. They are a constant feature in the adventitia of the capillaries and veins, which always show proliferation.

By the twentieth day the inflammatory reaction has changed greatly in character. In the epineurium there are many round or oval medium-sized nuclei of varying staining reaction. There are also numerous plasma-cells of which many are undergoing regressive changes; their nucleus and cell body are often pale, the halo is still perceptible, but the remainder of the cytoplasm is uniformly granular, and at the edge of the cell irregular. Occasionally at this stage the protoplasmic body is vaguely reticular. Side by side with these plasma-cells are numerous clear, hyaline, reticular cells with a small excentric nucleus frequently deeply stained. Young fibrous tissue cells are also present. Plasma-cells are very numerous in the perineurium and also in the adventitia of the veins which surround the nerve and pass into the septa between the bundles; they are typical morphologically, and are arranged in rows along the adventitia, whose nuclei are proliferated and stain rather feebly.

One inch above the upper end of the capsule there is in the sheath of the sciatic nerve a considerable diminution in the degree of inflammatory reaction. There are many proliferated nuclei in the epineurium, which are almost all oval in shape, and form small groups. Plasma-cells are rarely found lying free in the areolar spaces. The adventitial cells of the veins are enlarged, proliferated, usually oval in outline, and amongst them are many plasma-cells in all stages of development. These are not quite so large here as in the portion of nerve which lies on the capsule. Often their protoplasm is scanty, or irregular in outline, the halo narrow and more like a perinuclear ring; where several

are in apposition they may be cubical, but in all the cytoplasm is vaguely granular and the chromatin particles in the nucleus, which may or may not be central, are arranged in "clock-face" fashion. Associated with them are round nuclei rich in chromatin without a visible cell body, or with the merest trace. The endothelial cells of the veins are frequently swollen.

The veins and capillaries within the nerve are much less affected than in the perineurium, and the inflammatory reaction is of a more

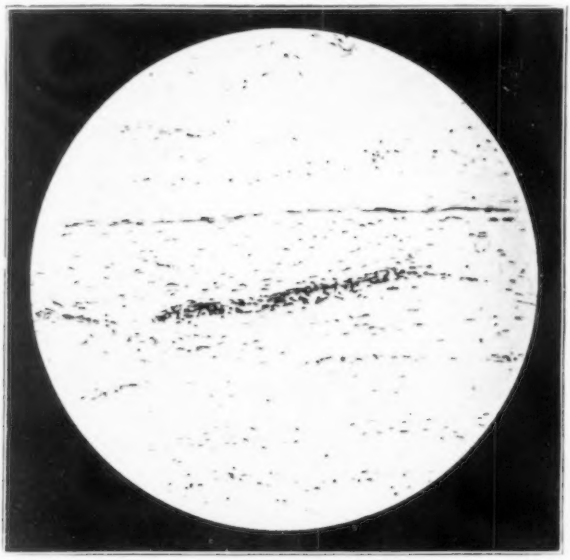

FIG. 6. Capillary within the nerve. Proliferation of adventitial cells.

sub-acute nature. The reaction in the capillaries is very variable, but always very definite (fig. 6). The adventitial nuclei are swollen, and in the spaces are many small, round, dark nuclei, around some of which is a moderate quantity of vaguely granular protoplasm; there is also a narrow perinuclear space. Quite frequently, and in connexion with the finest vessels, plasma-cell formation is the predominant feature. These are, as a rule, arranged in a row along the vessel wall, and exhibit all phases of transition from the youngest to the mature forms. The endothelial nuclei frequently show a considerable degree of swelling.

There is abundant evidence of irritation just distal to the sensory ganglia, in the ganglia themselves, and in the spinal roots of the lumbosacral enlargement. The nuclei of the cells of the ganglion capsule are swollen and in places proliferated. Round the veins there are groups of plasma-cells. These are also present in the adventitial sheath, whose nuclei are increased in number. A group of fully developed plasma-cells is often seen at the proximal pole of the ganglion just where the anterior and posterior roots diverge. Their relation to a vein is sometimes

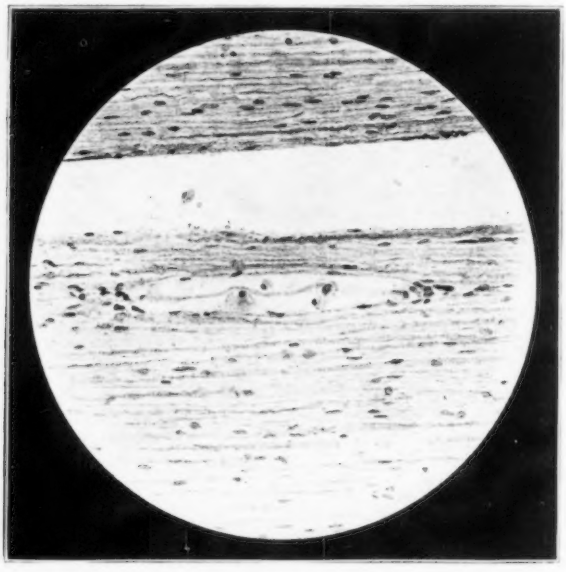

FIG. 7.—Posterior spinal root. Note the area of degenerate dmyelin. The axis cylinder is surrounded by compound granular corpuscles.

obvious, and hæmorrhage may be present with them. The capillaries of both roots and the ganglion show the same changes as described in the fasciculi of the sciatic nerve. The adventitial nuclei are proliferated, are round or oval, and in some the chromatin is arranged similarly to that in the nuclei of the plasma-cells of which there are many examples in all phases of development.

Chromatolysis of the ganglion cells is rare and when present is of the peripheral type. The nuclei of the nerve-cell capsule are proliferated, and at times invade the outer zone of the nerve-cell.

If we *summarize* the above phenomena we see an inflammatory reaction in the sciatic nerve which is continued through the sensory ganglia and along both spinal roots (fig. 7). The toxins induce inflammation of the fixed tissues, such as the epineurium, the perineurium, and in the veins and capillaries outside and inside the nerve; no reaction has been observed in connexion with the arterioles. There is a marked diminution in the severity of the inflammation as soon as the immediate neighbourhood of the toxic focus is left. The hæmatogenous elements do not participate in the process, and the very slight involvement of the intimal cells is noteworthy.

To put the cellular reaction briefly, we have, proceeding from the capsule:—

(1) A layer of polymorphonuclear leucocytes mixed with large clear nuclei.

(2) Developing and adult fibroblasts amongst which are clear nuclei similar to those in layer (1).

(3) In the epineurium, new vessel formation, clear nuclei of proliferating adventitia, round dark nuclei, and plasma-cells in all phases of development.

(4) In the inner layers of the perineurium a marked diminution in the degree of inflammation. The cells of the lamellæ are proliferated; there are many plasma-cells.

(5) One inch above the capsule there is much less reaction in both the epi- and perineurium.

(6) Within the nerve the inflammatory phenomena are very slight as compared with those in the nerve-sheath. Plasma-cell formation, especially in connection with the capillaries, is the most prominent feature. Similar vascular changes are seen in the posterior root ganglia and spinal roots.

In the polymorphonuclear layer and in the epineurium there are many reticulate cells. Many of the plasma-cells show regressive phases; their cell body becomes pale and hyaline, while the nucleus undergoes shrinkage.

### *B.—Where Suppuration occurred.*

When through rupture of the capsule the organisms escaped there was most intense inflammation of the nerve. The layer next the capsule is composed of groups of organisms, polymorphonuclear leucocytes, many of which are degenerate, and numerous cells with a large clear nucleus surrounded by a varying quantity of protoplasm. Outside this

layer there is a broad band of fibroblasts arranged in parallel rows, and in the epi- and perineurium a high degree of proliferation in the fibrous structures and vessel-sheath.

The proliferative reaction in the nerve-sheath decreases from without inwards. In the inner layers the laminar arrangement of the fibrous tissue is maintained, though the cells are elongated and swollen. In the outer layers the cells assume a variety of shapes. Some are elongated, in others the protoplasm shows no definite edge and lies to one side of the nucleus. Sometimes the protoplasm is collected in a mass round a central nucleus, or the nucleus may be excentric and the protoplasmic body possess several processes streaming away from it. There are many new formed vessels, some of which can be traced from the epineurium almost to the capsule. Their walls consist of one or more layers of elongated cells, with a pale fusiform nucleus and some protoplasm streaming from either side of it. Some of these cells are actively proliferating and wander into the surrounding tissue. Plasma-cells are few, and are seen only in the neighbourhood of the vessels of the epineurium.

In sections of the nerve just above the site of the capsule there is still proliferation of the epi- and perineural sheaths, but it is less active. Cell proliferation in the walls of the vessels is a striking feature, but it is limited to the veins and capillaries. The adventitial sheath shows the most pronounced change. The intimal cells are swollen, and in the majority the nucleus is pale and fusiform. At times, however, they are rounded and project into the lumen. With this the whole cell stains more deeply than normal. Multiplication by direct division may be observed frequently. As mentioned above there is marked proliferation of the adventitial elements. The nucleus is usually pale and oval, and the protoplasm may be concentrated around it or extend outwards on each side. Some assume the characters of fibroblasts and pass from the vessel wall into the fibroblast layer. Amongst the proliferating adventitial cells another type is evident. It possesses a rounded and deeply stained nucleus whose chromatin is uniformly distributed or arranged around the nuclear membrane. The protoplasm may be scanty, lie to one side of the nucleus or surround it, and be separated from it by a clear zone. Other cells show all the morphological characters of the adult plasma-cell, and these with their intermediate forms occur in large numbers in the adventitia of all the veins and capillaries, and also amongst the fixed connective tissue cells of the areolar tissue in the epineurium (fig. 8).

Two inches above the seat of maximum intensity there is a decided change in the character of the reaction. The adventitial sheath of the veins is filled with plasma-cells at different stages of development, and the intimal cells may be normal or show a slight degree of swelling. In the capillaries the intimal reaction is often more prominent than in the veins. Many of the plasma-cells show retrograde change in which the nucleus is small and darkly stained, while the protoplasm is hyaline, vacuolated, or reticulate.

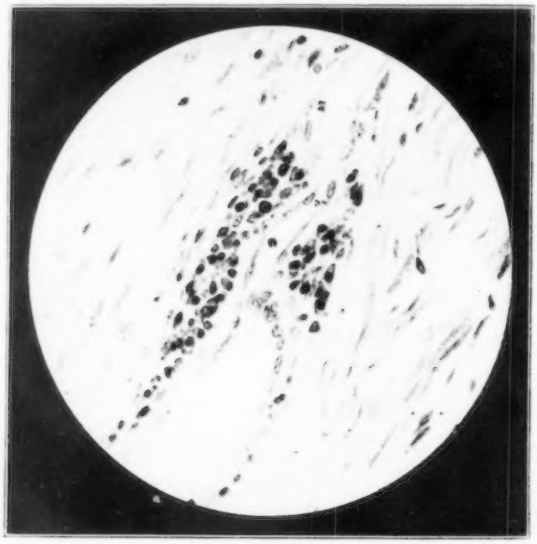

FIG. 8.—In the centre, plasma-cells round a venule of the perineurium; at the edge, young fibroblasts.

In the posterior root ganglia the capsular cells round the nerve-cells are increased in number, and the nerve-cells exhibit various stages of chromatolysis, or coagulation necrosis with homogeneous atrophy of the nucleus.

The appearances in B differ broadly from A in the much greater formation of fibroblasts, the larger number of new formed vessels, and the greater degree of reaction in both adventitia and intima.

*Series* 2.—In this series of experiments the capsule containing organisms was placed in a position much nearer the cord in order to

diminish the distance along which infection had to travel to it. The *Staphylococcus pyogenes aureus* was employed and two situations were selected for operation. In one the spinal cord was laid bare at the level of the lumbo-sacral enlargement and a capsule was fixed against the dura mater; in another the muscles were separated from the vertebræ in the dorsal region and a capsule placed against an intervertebral foramen. All the experiments gave positive results, which varied, however, in degree, as in some the capsule ruptured and the organisms spread to the dura mater.

The rabbits operated on lived for a period varying from three days to three weeks. The spinal cords were fixed in absolute alcohol for the toluidin blue and pyronin-methyl-green stains, and in Weigert's chrome-alum-copper solution for the Alzheimer and Mallory stains. The tissues were examined in transverse and longitudinal section.

In our description we begin with the reaction in the capsule of the posterior root ganglia and the dura mater, with which it is continuous; then, passing inwards, take up the inflammation in the spinal roots, the pia-arachnoid, the white and grey matter of the spinal cord. Longitudinal sections are especially useful in tracing the reaction from without inwards, because it is possible in the same section to compare the degree of intensity of the inflammatory process between one part and another in unbroken continuity from the sensory ganglion to the centre of the spinal cord. It will be seen that the reaction diminishes from without inwards, and that the dura mater and perineurium with their covering of highly vascular areolar tissue form a most efficient protection to the spinal cord and neutralize the effects of infection to a considerable extent.

### *A.—Where no Suppuration occurred.*

It is not necessary to describe the reaction in the ganglion capsule and the dura mater separately, as they are continuous. The inflammatory changes could be followed along the areolar tissue lying on the ganglion surface, and thence on to the outer surface of the dura. The spaces of the epidural tissue are filled with inflammatory products, the vessels are widely dilated, and there are hæmorrhages. The greater proportion of the exudation is composed of round mononucleated cells, amongst which are scattered the residue of degenerated polymorphonuclear leucocytes. The cell body of the mononuclears stains deeply with toluidin blue and intensely red with pyronin-methyl-green: it is round in the majority, oval in others, and the contour is irregular in

practically all. Its peripheral portion stains more deeply than the centre, and vacuolation is a constant feature. Many of these cells show advanced phases of degeneration in which the cytoplasm is reduced to shreds and the nucleus is pale and distorted.

The appearance of the nucleus varies very considerably. Sometimes it is small and deeply stained, at others it is larger and clearer. It may be central or excentric. The arrangement of the chromatin is not constant: in some nuclei it is situated round the membrane, in others it

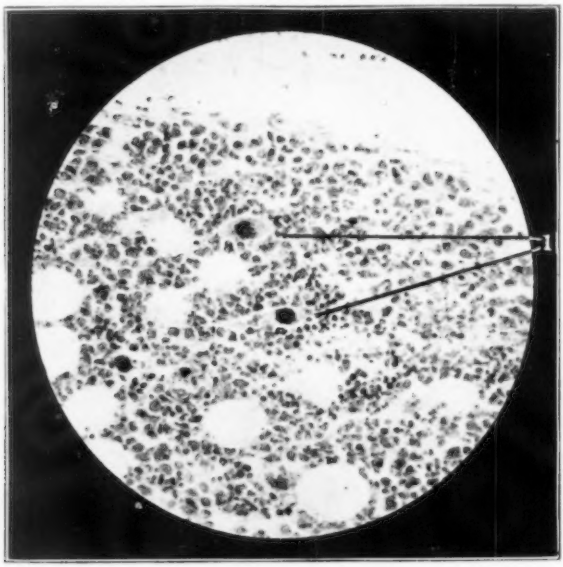


FIG. 9.—Inflammatory reaction in the epidural tissue: polyblasts, lymphocytes, reticulate cells, &c.; 1, giant cells.

is scattered throughout. Degeneration of these nuclei is common, when they stain diffusely and are irregular in outline. There are a large number of cells resembling small lymphocytes present, and compound granular corpuscles, with the typical fenestrated cytoplasm and the small dark excentric nucleus. Between the latter and the mononuclear cells there are many transitional forms. Mitotic figures occur in some of the cells, and giant cells are found in considerable numbers (fig. 9).

The adventitia of the veins of the epidural tissue is infiltrated with plasma-cells, all of which, however, are not fully developed. Here and

there around the veins are small collections of cells resembling lymphocytes. The nuclei of the areolar tissue cells are pale and swollen, and where the fibrous strands meet one often sees cells whose body is rounded and shows a small halo on one side of the nucleus.

Very distinct evidence of toxic invasion of the dura mater and ganglion capsule is seen from the presence of numerous plasma-cells between the fibrous tissue layers, and in the adventitial lymph spaces of the veins (fig. 10). There are no polymorphonuclear leucocytes or

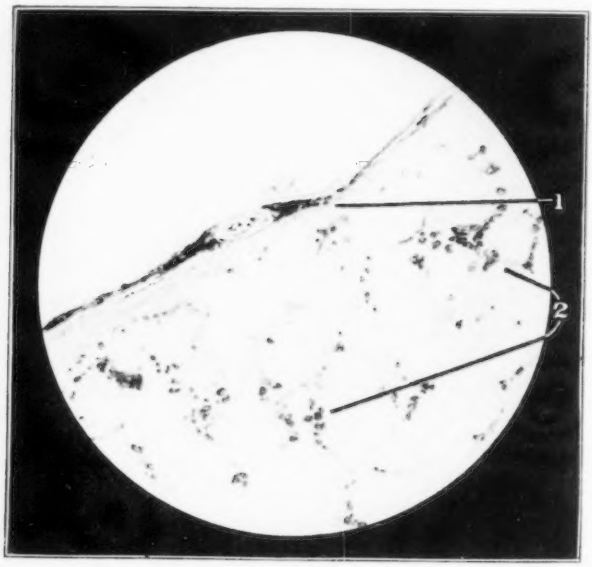


FIG. 10.—1, collection of plasma-cells round a vein in the dura mater; 2, proliferation of trabecular cells of epidural tissue.

mononuclear cells present. Many of the nuclei of the dural cells are swollen and oval in shape, and, from these, plasma-cell formation can be traced through transitional forms. Within the root ganglia there are many plasma-cells lying free, collected into small groups, or in the adventitia of the veins and capillaries. The reaction phenomena are greater in degree at the proximal pole of the ganglion where there is a large group of plasma-cells at the point where the spinal roots diverge (fig. 11). Their relation to a vein and to hæmorrhage in this situation is noteworthy. At this point and along the anterior and posterior spinal roots

inflammatory changes of varying degree are present in the adventitial sheath of the small veins and capillaries, and in the perineurium there are chains of plasma-cells extending from the ganglion to the spinal cord (fig. 12). The adventitial nuclei show signs of reaction. They diminish in size and become rounder and darker. As the cytoplasm increases in quantity the nucleus stains less deeply. Scattered amongst the adventitial nuclei are adult plasma-cells.

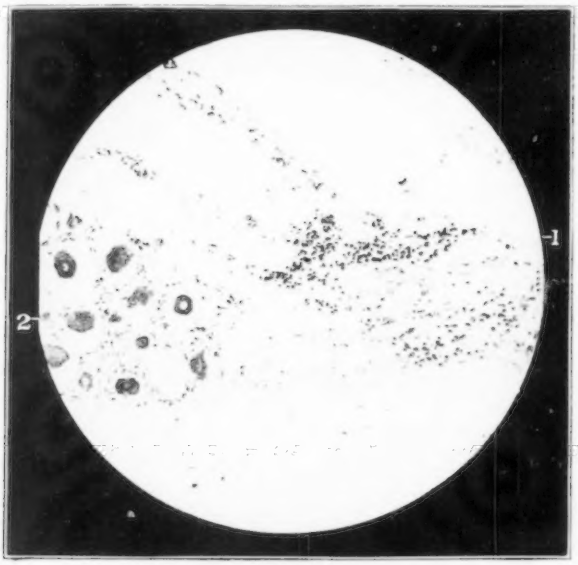


FIG. 11. -1, collection of polyblasts and plasma-cells at the proximal pole of the root ganglion; 2, root ganglion nerve-cells.

The degree of reaction in the pia-arachnoid and cord is much less than in the ganglia and spinal roots, and from the pia inwards there is a progressive diminution in the intensity of the inflammatory phenomena. The nuclei of the cells lining the trabeculæ of the pia mater are in many instances swollen and stain more deeply than normal. The adventitial cells of the veins and capillaries are greatly increased in number, are small, round and deeply stained, while plasma-cells in all stages of development are evident. This reaction is especially well seen in the small vessels passing from the inner layer of the pia into the white matter. In transverse sections vessels showing these

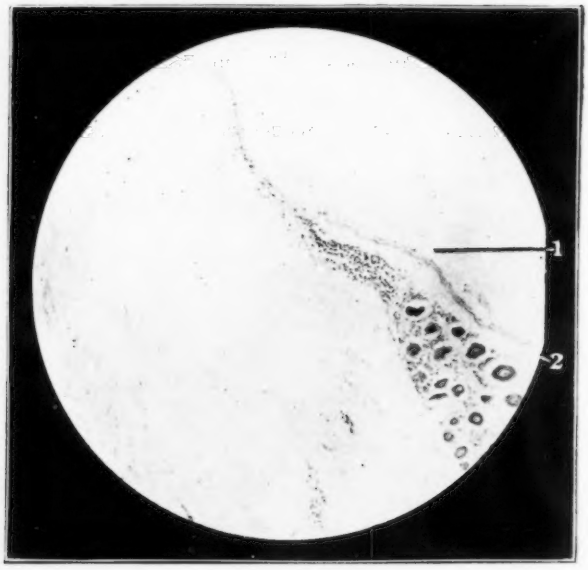


FIG 12.—1, inflammatory reaction in the perineurium between the root ganglion and the cord; 2, root ganglion nerve-cells.

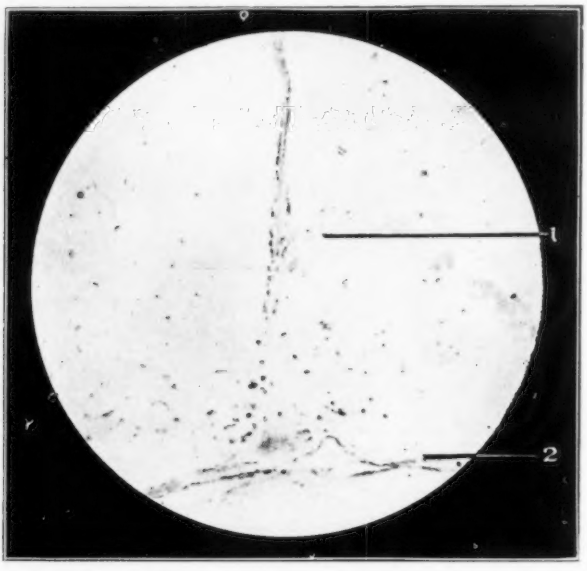


FIG. 13.—1, plasma-cells in the adventitial sheath of the vein in the postero-median septum of the cord; 2, pia-arachnoid.

changes are observed dipping into Lissauer's tract, the substantia gelatinosa Rolandi, the root entry zone, along the postero-median fissure, down the septa into the lateral region as far as the basis bundles, and through the area of the emerging anterior roots (fig. 13). Reaction changes are found in connexion with the vessels of the grey matter also, but trifling as compared with those of the peripheral portions of the spinal cord. The adventitial sheath of the veins and capillaries in the outer portion of the grey matter exhibits proliferative changes and is infiltrated with young plasma-cells, but near the central canal the reaction

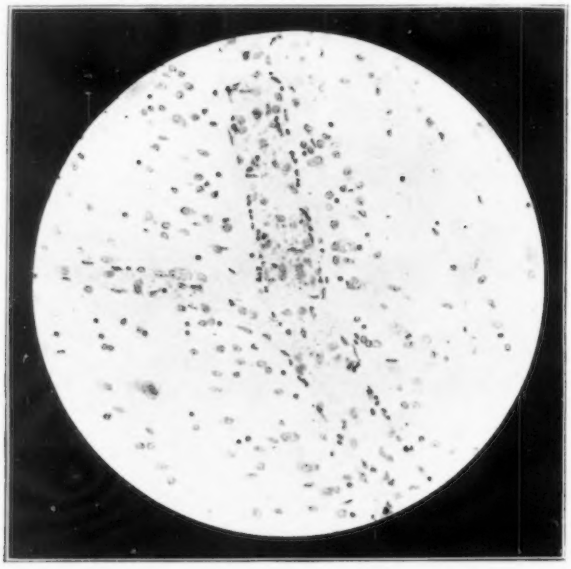

FIG. 14.—Note the proliferation of neuroglia round the venule.

is minimal. Here the adventitial nuclei are merely rounder and more deeply stained than normal, while at times the endothelium projects into the lumen.

The neuroglia elements throughout the cord are proliferated, especially in the neighbourhood of the venules and capillaries in the white matter. By Alzheimer's method the nucleus is clear, round or oval; the cytoplasm stains light blue, is increased in quantity, and often extended into short stumpy processes. These are the "amœboid" glia-cells which are characteristic of acute morbid processes. In toluidin

blue sections the proliferation of glia around the vessels is seen to be going on actively. A longitudinal section of a vessel shows a healthy endothelium, or nearly so, an adventitial sheath filled with darkly stained nuclei and young plasma-cells, and, separated by a clear space, a row of proliferated "amœboid" cells (fig. 14). In the grey matter the glia shows much the same change as in the white. The cells sometimes form small collections of four, five or even ten elements in the vicinity of the nerve-cells.

The large majority of nerve-cells are normal. No change is to be observed in the large cornual cells, but some of the smaller are pale and exhibit chromatolytic change. There is little change in the nerve-cells of the posterior root ganglia. In some there are regressive alterations of a mild nature and a few are invaded by round or oval clear nuclei. The cells lining the central canal are not affected.

The reactive changes induced by this series of experiments may be summarized briefly as follows:—

(1) In the epidural tissue; polymorphonuclear leucocytes, plasma-cells, and mononuclear elements similar to those termed polyblasts.

(2) Plasma-cells in the dura mater; in the capsule of the posterior root ganglion and within it where they form a prominent group at the proximal pole; in the perineurium of the spinal roots and in the adventitial sheath of their vessels; in the pia mater, and in the adventitial sheath of the vessels passing into the spinal cord.

(3) Proliferation of the neuroglia-cells.

*B.—Where Suppuration occurred.*

In the experiments in which a capsule was placed against an intervertebral foramen the organisms escaped and an abundant growth occurred in the surrounding tissues. From the site of the capsule the organisms could be followed along the nerves to the posterior root ganglia and onwards to the dura mater. The spread of the organisms was accompanied by active proliferation of the cells of the perineurium and a leucocytic exudation. The majority of the cells were degenerated.

There are many organisms in the areolar tissue covering the ganglion capsule and the dura mater. Here the inflammation is intense. The cells of the ganglion sheath, of the dura mater, and of the adventitia of the veins in those tissues are proliferating actively (fig. 15). Some of the proliferated cells have all the characters of fibroblasts, in others the nucleus is more rounded and the cell body larger. Others again,

with a paler nucleus, resemble large lymphocytes. Many degenerate forms are present. There is a high degree of proliferation of the capsular cells round the nerve-cells of the spinal ganglia, which exhibit acute chromatolytic changes.

The pia-arachnoid is acutely inflamed, and the cells of the exudate have an elongated oval shape and a nucleus moderately rich in chromatin. In the adventitia of the veins at the margin of the cord the reaction cells are rounder and their nuclei show variations in shape and

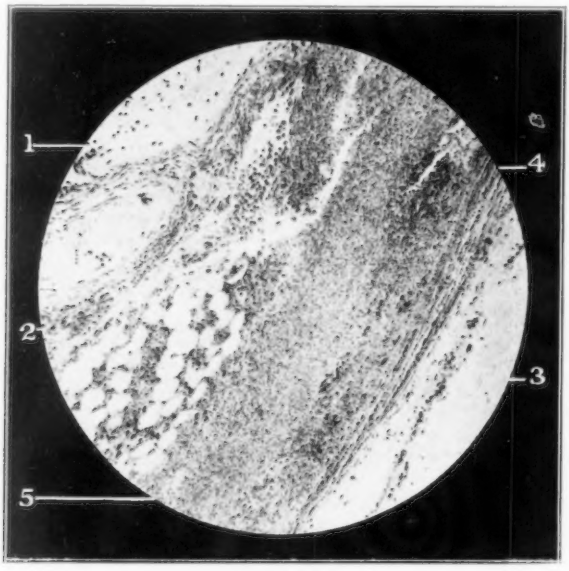


FIG. 15.—Inflammatory reaction outside dura. 1, posterior spinal root; 2, proliferation of cells of adventitia of a perineural vein; 3, lateral column of spinal cord; 4, proliferated cells of dura mater; 5, inflammatory reaction and organisms in epidural tissue.

staining quality. The majority of the nuclei are pale; a few are deeply stained. At times they are round, but generally oval, with an indentation on one side. Most of the cells possess a considerable quantity of protoplasm, but those with a round dark nucleus have little, and resemble small lymphocytes (fig. 16).

The efficiency of the dural barrier to the inward spread of organisms is well illustrated in these experiments. Only rarely did they reach the pia-arachnoid. When this did occur the organisms could be traced into

the adventitia of the veins of the lateral columns of the cord. A vein thus infected shows many degenerated cells in its adventitia close to the pia-arachnoid. Further inwards the reaction cells are better preserved and both adventitial and intimal cells are in a state of active proliferation (fig. 17). Their nuclei are round or oval, and in many cases show an indentation on one side; the cell sometimes contains a few irregularly distributed, deeply stained masses. Frequently the nucleus

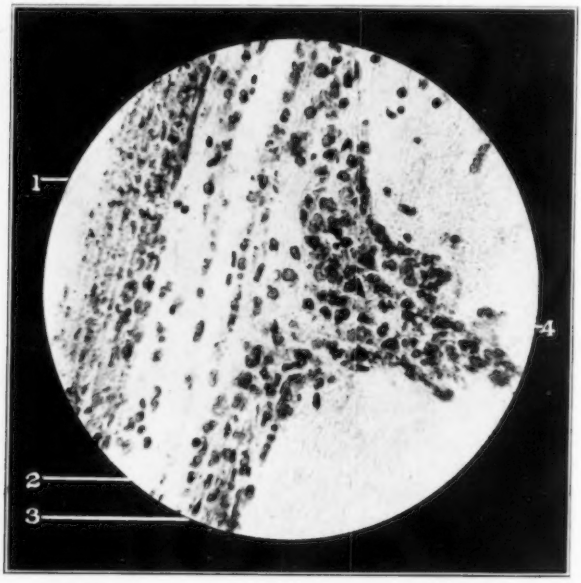


FIG. 16.—1, Organisms in epidural tissue; 2, proliferation of cells of dura mater; 3, proliferation of cells of pia-arachnoid; 4, proliferation of adventitial cells of a vessel passing into the lateral columns, with formation of polyblasts.

is so much indented and irregular in form as to resemble that of a polymorphonuclear leucocyte. Cells of this type have been described by Wickmann [43] in his work on acute poliomyelitis as "polyblasts."

In connexion with some of the vessels there are collections of cells which present quite a different appearance. Their nucleus varies in size and staining reaction. Most are round, deeply stained, and situated at one edge of the cytoplasm, which also shows variations. Frequently it is obviously reticulate, and the spaces in the meshwork may be clear, or occupied by a material which stains somewhat less deeply than the

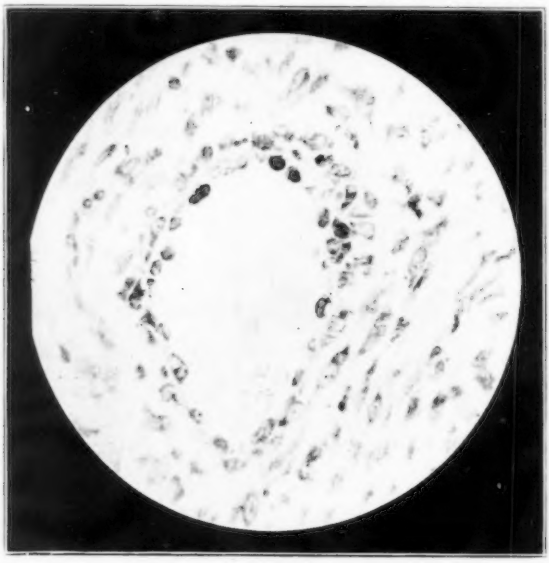

FIG. 17.—Proliferation of intimal cells, showing their projection into the lumen of the vessel.

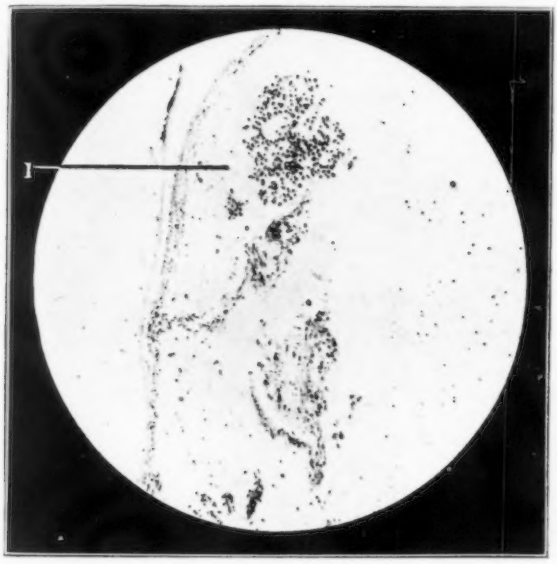


FIG. 18.—(1) Collection of compound granular corpuscles.

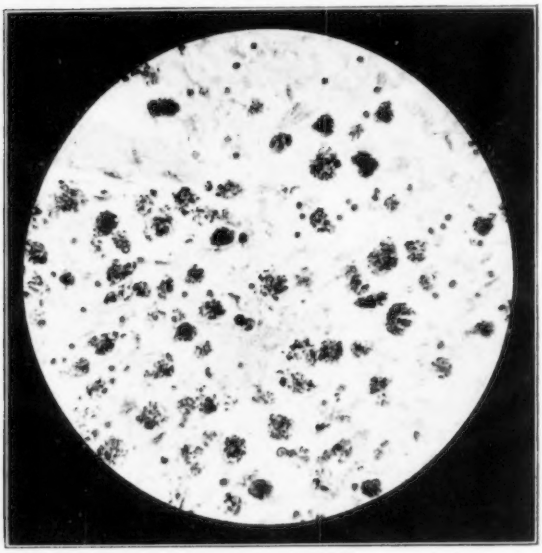

FIG. 19.—Compound granular corpuscles. (Körnchenzellen.)

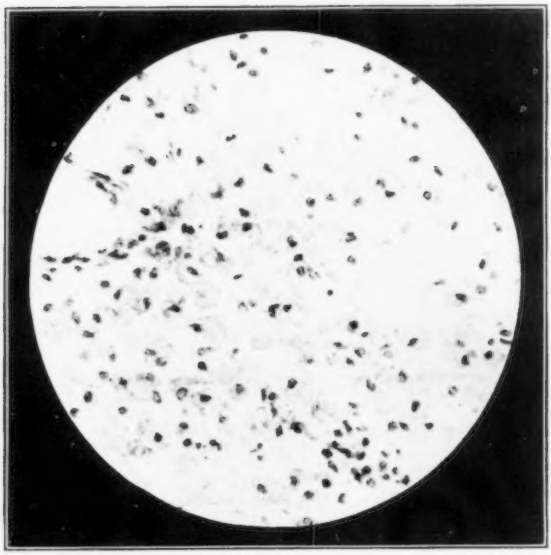

FIG. 20.—Reticulate cells.

nucleus. These cells correspond morphologically with the epithelioid cells and "Körnchenzellen" of Friedmann [11] and their function is that of removing the products of degeneration. Their significance will be discussed later (figs. 18, 19, 20).

Although it is rare to meet with organisms within the spinal cord, it is important to note that the vessels in both grey and white matter are the seat of marked pathological changes. They are dilated, and their walls are infiltrated with round cells (fig. 21). In some there are fibrin filaments. Hæmorrhages are seen occasionally. The infiltration of the vessel walls is more pronounced in the white matter;

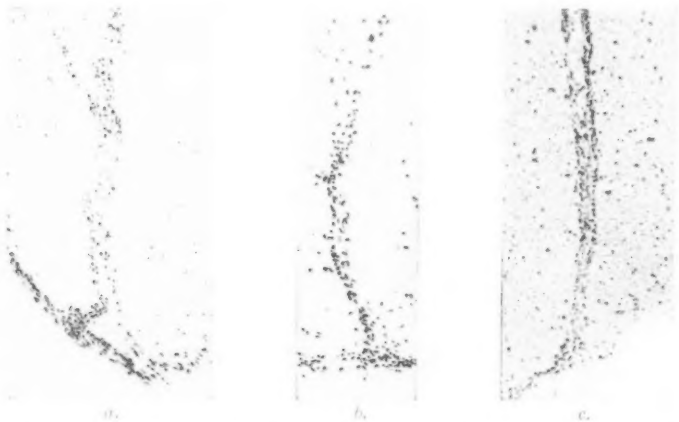

FIG. 21.—Three vessels showing adventitial proliferation: *a*, from experimental lymphogenous infection (cord); *b*, from a case of erysipelas of the face with ascending perineuritis of the fifth nerve (pons); *c*, from experimental acute poliomyelitis in the monkey (cord).

many of the small vessels in the grey horns show only a degree of dilatation and swelling of their endothelial nuclei.

There is a general neuroglia reaction particularly marked around the vessels, and the cells show transitional forms between the normal cell and the "amœboid" type of Alzheimer [3] (fig. 22). The nerve-cells are acutely degenerated. The majority stain very faintly and diffusely; in some the cytoplasm is in a condition of coagulation necrosis with homogeneous atrophy of the nucleus (fig. 23). Many of the nerve-cells are greatly disintegrated and neuronophagy is common. By Marchi's method there is evidence of much fibre destruction in the lateral columns of the cord.

FIG. 22.—Reaction of neuroglia cells: amœboid type of Alzheimer.

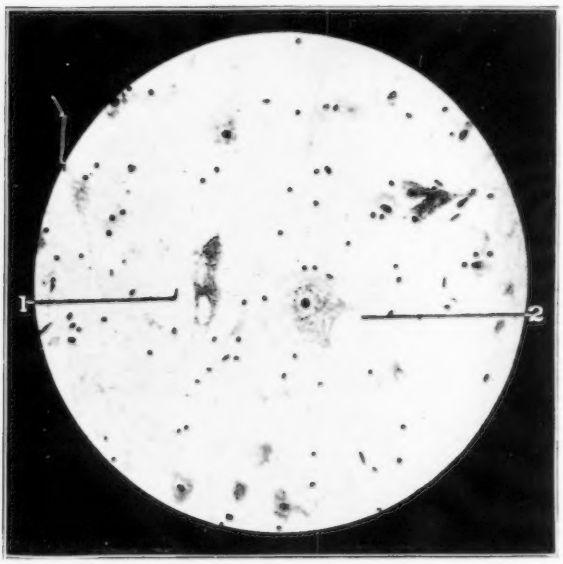


FIG. 23.—(1) Vacuolation of nerve-cell; (2) homogeneous atrophy of the nucleus.

On comparing the phenomena in B with those in A, we find that although they differ very considerably in degree, they have one feature in common, viz., the anatomical distribution of the inflammation.

The evidence given in Series I and Series II leaves no room for doubt that the lymph-stream in nerves is an ascending one, and that toxins and organisms can be carried to the cord by that path. The reaction of the tissues to the toxin also shows that the lymph not only ascends in the spaces of the nerve-sheaths, but diffuses in the fibrous septa between the nerve fasciculi and into the adventitia of the vessels. From the experiments, too, it is clear that when the toxin gains the spinal cord it is carried round the periphery in the meshes of the pia-arachnoid and along its prolongations into more central parts. It is exceedingly interesting to observe how the character of the inflammation undergoes progressive changes from the focus of greatest intensity onwards; and there is one important fact to which we would draw attention and that is how plasma-cell formation becomes the most prominent indication of irritation when the irritant has been to a great extent neutralized by the reaction of the tissues close to the capsule.

The proliferation of the adventitial sheath of the veins and capillaries with plasma-cell formation shows that its lymph spaces communicate directly with the lymphatic system of the nerves and cord; and though, doubtless, the adventitial lymph system of the arterioles has a similar connection, yet the intense reaction around the veins and capillaries points to these as being the principal channel by which the lymph regains the general circulation. This opinion receives support from researches carried out by other methods, such as the injection of coloured fluids into the sub-arachnoid space; these find their way rapidly into the adventitia and thence into the blood-stream. According to Lewandowsky [17], the veins, capillaries, and Pacchionian bodies are the channels by which the cerebrospinal lymph is returned to the general circulation. The reason why the adventitia of the veins and capillaries of the nervous system in lymphogenous infection should show so much inflammatory change is therefore obvious.

The results of the above experiments show that infection of the lymph system of peripheral nerves is followed by an ascending perineuritis which spreads to the posterior root ganglia and along the spinal roots to the cord. The loose areolar tissue covering the perineurium, the ganglion capsule, and the dura mater shows the

greatest degree of inflammation. The *clinical cases* which we are now about to bring forward have confirmed the results of our experiments, and it will be observed that not only is the same path of infection clearly demonstrated, but also a perfect similarity in the type of reaction. This reaction varies with the degree of intensity of the irritant.

We propose to give here a digest of these clinical cases: a fuller account has appeared in a previous publication—written in collaboration with Dr. Stephenson [32].

(1) *Carcinoma of the tongue with suppuration in the floor of the mouth.*—The tissues examined microscopically were the twelfth, seventh and fifth cranial nerves; the pons and medulla; the spinal cord; the nerves and posterior root ganglia connected with its cervical portion. In the twelfth and seventh nerves there is a well marked perineuritis. The cells of the exudate possess a round or indented nucleus containing little chromatin, and a faintly stained cell body. Other cells are present with a deeply stained nucleus and a small quantity of well stained protoplasm. The cells of the adventitial sheath of the veins and capillaries in the epi- and perineurium are proliferated. In some of the capillaries the endothelial cells are swollen, round, and project into the lumen. Within the nerve the reaction is much less intense. The neurilemma cells are swollen, and plasma-cells are present in the adventitial spaces. Around the nerve-cells in the geniculate ganglion of the seventh nerve there is proliferation going on amongst the capsular cells. A perineuritis is still present at this level, though it is not so acute as in the more peripheral portion.

The highest degree of inflammatory reaction is round the fifth nerves outside the dura mater, and in the Gasserian ganglia. The peri- and epineurium are infiltrated with polyblasts and cells of the small round lymphocyte type. Between these two are transitional forms. There are also reticulate cells containing refractile granules which stain purple with toluidin blue. They are numerous where hæmorrhage and blood pigment are present, and are probably scavenger cells. Possibly these granules, which at times escape from the cell through the bursting of the cell membrane, correspond to the hæmosiderin observed by Bonfiglio [6] in plasmatocytes of the central nervous system.

Within the Gasserian ganglion there is less reaction than around the nerves. The polyblasts are fewer in number, and larger, rounded, well stained cells with a darkly stained nucleus are present. These resemble the pseudoplasma-cells of Pappadia [33]. Plasma-cells are

present; the capsular cells round the nerve-cells are proliferated and while some of the latter show coagulation necrosis with homogeneous atrophy of the nucleus, in others there is advanced chromatolysis and neuronophagy.

The degree of irritation in the pia mater covering the pons is much less than in the structures already described. There is infiltration with small round cells, some of which exhibit the characters of plasma-cells. The same appearance is seen in the adventitial sheath of vessels passing into the pons. The pontine vessels are markedly dilated: the nerve-cells show chromatolysis; and the neuroglia-cells are proliferated.

There is an intense perineuritis of the ganglia and spinal roots of the cervical region. The inflammatory phenomena are most evident in the epidural tissue and at the proximal pole of the ganglion. Within the dura mater the reaction is of less degree. The pia-arachnoid is infiltrated by lymphocyte-like cells, but some plasma-cells are present; the infiltration reaches its maximum in the cervical and upper dorsal regions. The vessels within the cord are dilated and their adventitial cells proliferated.

(2) *Erysipelas of the face.*—The disease ran a course of five days' duration. The fifth cranial nerve, the Gasserian ganglia, and the pons were examined. There is acute hæmorrhagic inflammation of the epi- and perineurium of the fifth nerve. The proliferated cells are mostly of the small lymphocyte type mixed with others possessing a larger, clearer nucleus and a fairly large cell-body. In the neighbourhood of the hæmorrhages are many cells with a small deeply stained nucleus and a large cell body filled with refractile purple granules. In the sheath of the Gasserian ganglia there are groups of micro-organisms, and here the perineuritis is very acute, the cell exudate showing various stages of reaction from the small round cell to the typical polyblast (fig. 24). Within the ganglia the reaction is less acute: the connective tissues and adventitial sheaths are proliferating. There is marked chromatolysis of the nerve-cells with homogeneous atrophy of the nucleus, and their capsular nuclei are greatly increased in number. In the pia-arachnoid of the pons there is a considerable degree of round-cell infiltration. Within the pons the vessels are dilated, while the walls of the veins and capillaries show signs of reaction. Chromatolysis is present in the nerve-cells; many of the neuroglial elements have undergone an acute reaction.

(3) *Juvenile general paralysis with bed-sores* over the sacrum, right

hip, and elbow; of three weeks' duration; there was necrosis of the gluteal muscles. At *post-mortem* examination there was great excess of cerebrospinal fluid. There was a purulent inflammation of the epidural tissue over the lowest portion of the cord. Microscopically the loose areolar tissue covering the dura contains micro-organisms, hæmorrhage, and the proliferated cells of the connective tissue. Some of the cells in the exudate resemble polyblasts, in others the nucleus is more deeply stained, and the surrounding protoplasm greater in quantity.

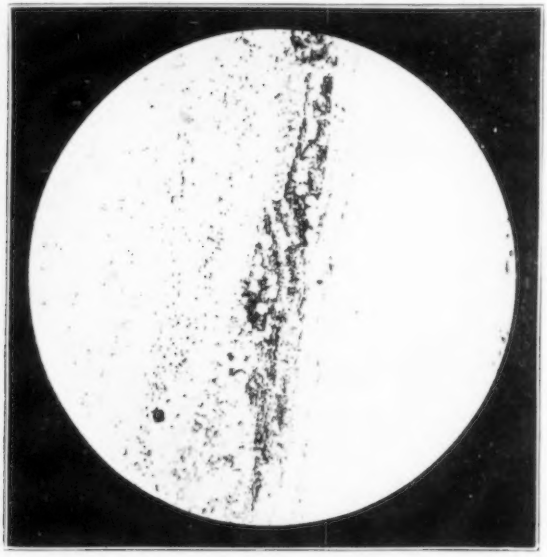

FIG. 24.—From a case of erysipelas of the face. Note the intense inflammatory reaction in the areolar tissue covering the sheath of the Gasserian ganglion.

Small, round, lymphocytic cells are also present. There are no organisms within the dura mater, but a considerable degree of inflammatory reaction. There is active proliferation of the cells in the perineural sheath of the spinal roots. Here are groups of cells resembling the pseudoplasma-cells of Pappadia. Within the nerves and sensory ganglia there is less reaction. The adventitial cells of the venules and capillaries have proliferated, and plasma-cells are present. The nerve-cells show chromatolysis, and their capsular cells are increased in number. The pia-arachnoid over the lumbo-sacral region is infiltrated

with small round cells. Within the cord there is proliferation of the adventitial sheath of the vessels, and neuroglia reaction. All the signs of irritation diminished from below upwards.

(4) *Tubercular nodules in pleura.*—The nodules were present on both parietal and visceral pleuræ, on the pleural surface of the diaphragm, and outer layer of the pericardium. The composition of a nodule was fibrous tissue, lymphocytes, connective tissue cells with large clear nuclei, and giant cells. No baciili were seen by the Ziehl-Nielson stain.

In the *dorsal cord* the endothelial nuclei on the inner surface of the dura are proliferated. The perineurium of the spinal roots and the septa are infiltrated with many lymphocytes and a few plasma-cells. The neurilemma cells are proliferated. The reaction is most marked where the nerves pierce the dura mater. The pia-arachnoid is filled with lymphocytes mixed with plasma-cells. Within the adventitial spaces of the vessels are many lymphocytes and some plasma-cells. Giant cells are present in the pia-arachnoid.

Within the cord the adventitial sheaths are infiltrated with lymphocytes, and cells with a large clear nucleus; plasma-cells occur occasionally near the cord margin. There is a considerable degree of neuroglia proliferation, and by Marchi's method much myelin degeneration scattered uniformly throughout.

In the *cervical region* there is a marked diminution in the degree of inflammatory reaction. The presence of giant cells in the pia-arachnoid is noteworthy. In the *lumbar cord* the adventitia of the vessels in the spinal roots is infiltrated with lymphocytes; these are also present in the pia-arachnoid, and giant cells are to be seen here in the vessel adventitia. Within the cord there are some lymphocytes in the external coat of the larger vessels, the endothelium of the capillaries shows proliferative changes, and the neuroglia cells are increased in number.

(5) *Tubercular lumbar abscess.*—The patient developed symptoms of acute meningitis two days before death. There are tubercle bacilli and giant cells in the wall of the abscess. In the *lumbar cord* the spinal roots are practically normal. The pia mater and adventitial spaces are infiltrated with lymphocytes: a few plasma-cells are present. Some giant cells are to be seen in the perivascular tissue. A mild degree of adventitial proliferation and neuroglia reaction is present within the cord.

In the *dorsal cord* the perineurium of the spinal roots shows a high degree of inflammatory reaction consisting of lymphocytes, proliferated

connective tissue cells, and plasma-cells. Rows of lymphocytes occur in the septa between the nerve-bundles. The neurilemma nuclei are increased in number, while the vessels are engorged and dilated. There is much proliferation of the cells of the pia-arachnoid, and its spaces are infiltrated with lymphocytes, as is the adventitia of its vessels. Plasma-cells also are present, and giant cells. Within the cord there are inflammatory changes in the septa and proliferative changes in the adventitia, which is filled with lymphocytes. There are hæmorrhages in the white matter, and in the fourth dorsal segment in Burdach's column near the cord periphery there is a small isolated patch of myelitic softening. The neuroglia is proliferated. Marchi's method shows diffuse myelin degeneration more prominent round the cord periphery. Myelin degeneration is also present in the spinal roots.

In the *cervical cord* the inflammatory reaction in the pia-arachnoid is quite well marked, but of less degree than in the dorsal region. Giant cells are present in the vessel adventitia. The perineurium of the spinal roots shows the same type of reaction as in those of the dorsal cord.

(6) *Cancer of œsophagus* at the level of the crossing of the left bronchus. The tumour was epitheliomatous and was ulcerated. In the *cervical cord* the epidural tissue is greatly inflamed. There are hæmorrhages, micrococci arranged in pairs or short chains, and many degenerated cells—in all probability polymorphs. In the dural tissue are cocci, polymorphs, and some mast-cells. The perineurium of the spinal roots is infiltrated with small round cells; these are also present in the septa between the nerve-bundles, and in one anterior root there are cocci similar to those in the dura lying amongst the reaction cells. The neurilemma nuclei are proliferated, as are the capsular cells surrounding the posterior root ganglion nerve-cells. These show acute chromatolysis and are almost devoid of chromophile material. There are small groups of cocci in the pia-arachnoid, and many degenerate polymorphs, lymphocytes, and proliferated connective tissue cells. Within the cord the vessel adventitia is greatly proliferated; lymphocytes are few in number, and there are no plasma-cells. The neuroglia shows signs of reaction: the nucleus is swollen, rich in chromatin, while the enlarged cell body is branched.

In the *dorsal cord* the dura mater is normal. The pia-arachnoid is infiltrated with many polymorphs and to a less degree with lymphocytes. The perineural sheath of the spinal roots contains many polymorphs; the connective tissue cells and adventitial elements are proliferated; the vessels are dilated and congested; the neurilemma is normal. Within

the cord there is a high degree of adventitial proliferation mixed with small, round, lymphocyte-like cells. The endothelial cells of the capillaries are swollen and proliferated. Small hæmorrhages are frequently seen, and the neuroglia cells especially at the cord margin are of the proliferated "amœboid" type.

In the *lumbar region* there are many polymorphs in the pia-arachnoid; lymphocytes are present in somewhat fewer numbers. Here the vessels are engorged, and also in the spinal roots, whose fibrous sheaths are filled with both polymorphonuclear leucocytes and lymphocytes. In both pia and spinal roots there is a moderate degree of adventitial proliferation; the neurilemma is normal. Within the cord the vessels are engorged, and a very few lymphocytes are present in the adventitial spaces. There are small hæmorrhages in the grey matter.

In the *medulla*, *pons*, *cerebellum* and *cerebrum* there are inflammatory phenomena similar to those described above.

(7) *General paralysis of the insane with empyema of right pleural cavity and herpes zoster on the same side.*—The fourth, fifth and sixth right intercostal nerves were examined. The inflammatory exudate in the epineurium shows the same distribution as has been noted in nerves infected experimentally. Its character is subacute and consists in lymphocytes, plasma-cells, fibroblasts, and mast-cells. The cells of the trabeculæ between the nerve-bundles are proliferated. The large majority of the plasma-cells are degenerate, and many resemble compound granular corpuscles. Many of the mast-cells are similar in appearance to the so-called clasmatocytes of Ranvier. The adventitial elements of the veins and capillaries are proliferated and many plasma-cells are present in the spaces.

The connective tissue of the perineurium and its septa has proliferated to form fibroblasts. There is adventitial proliferation in the veins and capillaries. The neurilemma nuclei are swollen, round and pale, while the protoplasm contains numerous lilac-coloured granules (Reich's corpuscles).

Within the right fourth dorsal posterior root ganglion there is a sclerotic area surrounded by a zone of small round-celled infiltration. A similar type of exudation is present in the layers of the ganglion capsule and around its vessels. Two-thirds of the medullated fibres of the corresponding posterior root are degenerated and the neurilemma nuclei proliferated. The cord was examined by Marchi's method and in the fourth dorsal segment there was degeneration in the root entry zone.

The degeneration of this root was traced as far as the third cervical segment.

All these cases except the last one show a diffuse meningo-myelitis of the cerebrospinal axis, the result of toxi-infection of the peripheral nerves. The inflammatory phenomena in the cord and its membranes vary in intensity from case to case according to the potency of the infective agent, and the spread of the inflammation is by the direct continuity so typical of lymphogenous infection. The cases show that any portion of the central nervous system may be attacked by organisms or toxins passing up the nerves from infective foci, and although the morphological changes may vary according to the potency of the exciting cause the anatomical path of entrance and spread is a constant one.

We have already demonstrated how in experimental infection of the lymph-stream of nerves certain structures invariably show the greatest degree of reaction, and the above clinical cases confirm this. These structures are the loose areolar tissue covering the nerve-sheath and the dura mater, and the adventitia of the veins and capillaries. In both the peripheral nerves and cerebrospinal axis the degree of reaction diminishes from without inwards and that portion of the latter directly connected by nerves with the peripheral source of infection exhibits the highest degree of inflammation.

So far we have dealt only with lymphogenous infection of the cord and brain. We shall now contrast the lesions produced by this mechanism with those which occur when a hæmatogenous intoxication is induced.

We have lately undertaken a series of experiments in which the abdominal cavity was chosen as the site for infection. This was done for three reasons: (1) The peritoneal cavity is most suitable for an experiment in which one wishes to avoid infection of the lymph system of spinal nerves; (2) to reproduce as closely as possible a gastro-intestinal intoxication, and observe the effects upon the spinal cord; (3) to ascertain in how far such toxi-infection affected the sympathetic ganglion chain. Celloidin capsules containing a broth culture of the *Staphylococcus pyogenes aureus* were therefore placed in various regions of the abdomen where they became attached to the mesentery, kidney, bladder, or lower border of the stomach. The number of capsules introduced

varied from two to six, and the animals were permitted to live for from three to six weeks. Ten rabbits were used and one dog.

At *post-mortem* examination the capsules were found surrounded by an inflammatory exudate, and the vessels of the mesentery, stomach, small and large intestines were much engorged. The inflammatory reaction extended from the neighbourhood of the capsules a considerable distance along the mesentery, and there was abundant microscopical evidence of reaction in connexion with the sympathetic ganglia. Some of these were surrounded by masses of degenerate polymorphonuclear cells, by cells of the lymphocyte type, and by fibroblasts; the vessels passing into the ganglion substance showed proliferative changes in the adventitia. There was chromatolysis of the ganglion nerve-cells, which was central in type, with displacement of the nucleus to the periphery.

The spinal cords were fixed in formalin and bichromate of potassium, and pieces from all regions were cut in longitudinal and transverse section. There was no evidence of lymphogenous invasion either in the sheath of the spinal ganglia, the perineurium of the spinal roots, or in either the dura mater or pia-arachnoid. The posterior root ganglion cells were normal but their capsular cells showed a slight degree of proliferative change.

Within the cord the picture was remarkably different, a most striking feature being the proliferation of the glial elements, which affected both grey and white matter, but especially the outer layers of the latter. The hypertrophied cells were of the amœboid type and frequently formed a row of elements lying end to end. No karyokinetic figures were seen. Some glial elements had undergone regressive change in which the cytoplasm assumed the reticular appearance of a compound granular corpuscle. Many amœboid neuroglia cells clustered thickly round the veins and capillaries of the white matter; while the signs of morbid change in the adventitia and intima consisted only in a slight degree of deformity of the nuclei. This contrasts sharply with lymphogenous inflammation where adventitial proliferation is constant. In addition to this generalized neuroglia reaction there were small scattered sclerotic foci consisting of glial elements in the resting stage following proliferation. Their nuclei were smaller than normal, filled with chromatin, and their cell bodies and processes massed together to form a syncytium. They occurred most frequently in the neighbourhood of the cord margin, and at times were definitely related to dilated vessels and hæmorrhages. Numbers of cells of the lymphocyte type were seen in both grey and white matter in some of the experiments.

The nerve-cells showed early chromatolysis. In some the nucleus was rather diffusely stained, an appearance suggestive of the initial stage of homogeneous atrophy, and the chromophile elements in the cell centre had an increased affinity for the stain, while their edges were not so sharply outlined as in the normal. In other cells the elements at the edge of the cell body were disintegrated. There were many cells of the lymphocyte type scattered amongst the nerve-cells and often lying in close proximity to them. Many swollen neuroglia nuclei were found round the margin of the nerve-cells.

Portions from the cervical, dorsal and lumbar levels of the cord were examined for alterations in the myelin sheath. The Marchi, Wolters, and Donaggio methods were employed, and all gave positive results. The latter method was found to be the most trustworthy for demonstrating the early changes in the myelin sheath. The striking feature of the medullated fibre lesions was their non-systemic character. The two areas involved were the cord periphery and the posterior columns. In the cervical and lumbar regions the whole cord periphery was affected, leaving the pyramidal tracts and antero-lateral basis bundles free. In the dorsal cord this marginal degeneration did not involve the posterior columns. The degeneration of the posterior columns varied from region to region. In the lumbar cord it formed a small triangle round the posterior end of the postero-median septum with its base towards the cord margin. Higher up, in the dorsal cord, the degenerated fibres formed a V whose apex reached the middle of the septum, while its limbs diverged backwards towards the cord margin, leaving the area round the posterior third of the septum practically free from degenerated fibres. In the cervical cord the degenerated fibres were more numerous than in the lower regions and formed a narrow column situated slightly external to each side of the median septum and running backwards to join the marginal degeneration. The medullated fibre lesion was therefore maximal in the cervical and minimal in the lumbar region, and the root entry zones throughout the cord were free from degeneration.

Wolters' method showed no sclerosis in any of the tracts; but in the external portions of the cord the medullated fibres were swollen, irregular, and often fragmented, appearances resembling those found in the cord œdema of cancer cachexia and pernicious anæmia. By Marchi's osmic acid method some fibres scattered throughout all regions of the cord gave a positive reaction. In the vein of the postero-median septum the adventitial sheath sometimes contained a considerable quantity of degenerated myelin which had evidently been carried there by the lymph current.

The changes in connection with the vessels varied very considerably and were more evident when four or six capsules were placed in the abdomen. In some experiments nothing beyond an increased affinity for aniline dyes on the part of the adventitial nuclei, and some distortion of the intimal nuclei of the veins and capillaries was noticed. There were a few cells of the lymphocyte type in the adventitial lymph spaces. Where a higher degree of toxicity was induced the changes in the vessels were the most prominent feature. All the arteries, veins, and capillaries in both grey and white matter showed hyaline degeneration of their walls, and many contained partial or complete thrombi. In the vessels showing incomplete thrombosis the hyaline material lay along the vessel wall as a thick band connected by trabeculæ with a very definite hyaline network in the lumen. Many vacuoles were seen in the thrombi, and there was practically no disturbance of the intimal or adventitial nuclei. Morbid changes of somewhat the same nature have been observed by ourselves and Ziveri in senile dementia [45], by Campbell in general paralysis of the insane [7], and by Alzheimer [4] in general paralysis of the insane and epilepsy.

If we summarize the changes above described, we find (1) the most highly developed structures, the nerve cells, suffer least of all; (2) there is primary degeneration of the myelin sheath round the cord margin and along the postero-median septum; (3) the myelin degeneration is greatest in the upper part of the cord; (4) there is œdema of the cord; (5) there is active proliferation of the perivascular neuroglia; (6) the vessels are dilated, congested, are hyaline, and contain thrombi of the same nature. If these be now contrasted with the cord lesions in lymphogenous infection the difference is at once obvious. Lymphogenous infection is characterized by (1) the reaction of the cells of the fixed connective tissue; (2) the proliferation of the cells of the adventitial sheath of the veins and capillaries; (3) the appearance of numerous scavenger-cells when the myelin is disintegrated; (4) nerve-cell degeneration and neuronophagy. From the above one must conclude that the lesions in hæmatogenous intoxication are of a degenerative nature and differ very widely from those found in lymphogenous infection, where the fixed tissues are actively proliferating and all the morbid phenomena are of an inflammatory type. The difference between the two might, therefore, be expressed by saying that in lymphogenous infection the inflammatory phenomena reach their maximum; in hæmatogenous intoxication they are reduced to a minimum.

In giving a short preliminary account of these experimental hæmatogenous lesions, we feel that the term "hæmatogenous" requires qualification. We do not consider that the term sufficiently explains the mechanism of production. It would seem as though there was another factor at work. If we look at the distribution of the myelin degeneration alone for a moment, round the cord margin where œdema is present, and on either side of the postero-median septum, the explanation of a "general intoxication" is hardly sufficient. Weaker resistance on the part of the fibres in those situations might be put forward as a predisposing cause, but this suggestion cannot be substantiated.

Lesions of practically the same distribution are found in cancer cachexia, pernicious anæmia, Addison's disease, &c. It is of importance to note that the grey matter of the cord so richly supplied by the anterior spinal artery may be normal; Goll's tract in the cervical enlargement is attacked in its middle third, leaving the long lumbosacral fibres so far away from their trophic centre untouched: between the lesions in the cervical, dorsal, and lumbar cord there are great differences not to be accounted for by a focal lesion. Such a distribution of degeneration cannot be explained by a general intoxication. It fails completely when we consider that the areas supplied by the pial vessels, the cord margin and postero-median septum, show degenerative change, while the regions supplied by the anterior spinal arteries escape. It is highly probable that there must be another factor besides intoxication which determines the localization of the degenerations, and certain indications point to the sympathetic nervous system.

We have shown evidence of involvement of this mechanism in the inflammation round the sympathetic ganglia, the proliferative changes in the adventitia of their vessels, and in the chromatolysis of the nerve-cells; and when it is remembered that the cord lesion in abdominal cancer and Addison's disease—in both of which sympathetic reflex action must be considerably disturbed—have almost the same distribution as in our experiments, sympathetic influence cannot be excluded.

There is evidence in the vessels of the cord, too, of altered sympathetic action; in the dilatation, hæmorrhages with sclerosis, and in the hyaline thrombosis—all pointing to stasis. As to whether this stasis is due to toxic action upon the prevertebral chain or is caused by the direct action upon the cord vessels of a toxin in the general circulation, it is difficult to say. This latter suggestion seems improbable, as judging from the relative integrity of the nerve-cells and the minimal

reaction of the vessel endothelium within the cord, the toxicity of the blood-stream must have been very mild. In all probability both factors come into play. The disturbance of the sympathetic influence upon the cord vessels might be held responsible for a dilatation and increased permeability of their walls, so facilitating the passage of toxins into the surrounding tissues. Evidence of this is seen in the proliferation of the perivascular neuroglia. It is conceivable, however, that with time a permanent paresis of the vessel wall with slowing of the blood-current occurs, thus affording the most favourable conditions under which mild toxicity of the blood could exercise a deleterious action upon the vessel walls and nutrition of the nervous tissues generally. Whether we are right or not in attributing importance to the sympathetic factor must be left to further experiment. Our present position with regard to these hæmatogenous lesions is that the term "general intoxication" expresses their pathology inadequately.

From the above clinical and experimental study it is clear that the two mechanisms of infection of the cerebrospinal system—the hæmatogenous and lymphogenous—are characterized by sufficiently distinct morbid phenomena, and if we apply the results of the experiments to the human subject we obtain very considerable assistance in arriving at an understanding of the genesis of certain lesions.

We have brought forward ample evidence to show that acute and chronic myelitic conditions are readily produced by infection of the ascending lymph system in nerves. We have previously given it as our opinion that general paralysis of the insane is a chronic inflammatory disease of lymphogenous origin. This opinion is based on the close similarity between the vascular lesions in this condition and those found in our experiments where the lymph system of the nerves or cord is infected. The striking predominance of adventitial proliferation and infiltration can be explained only by toxi-infection of the cerebrospinal lymph. There is no evidence of a general blood intoxication, for in dementia paralytica, as in our experiments, the endothelium of the vessels may be quite unaffected, while the adventitial spaces are packed with the products of proliferation (fig. 25). Further, to tabes dorsalis we assign the same lymphogenous genesis. The vascular phenomena, similar to those in general paralysis, the constant primary affection of the root entry zones, and the rigidly systemic character of the lesion preclude any other conclusion.

We have shown that certain cases of acute meningo-myelitis fall into the lymphogenous category, and there is now a preponderance of evidence to show that acute poliomyelitis must also be included in this group. The whole picture of this disease is one of a disseminated meningo-myelitis, and as the brain may be affected in adults especially, the more comprehensive term of disseminated meningo-myelo-encephalitis has been suggested by Wickmann [43]. There are many facts which show that infantile paralysis cannot be a blood infection, and indis-

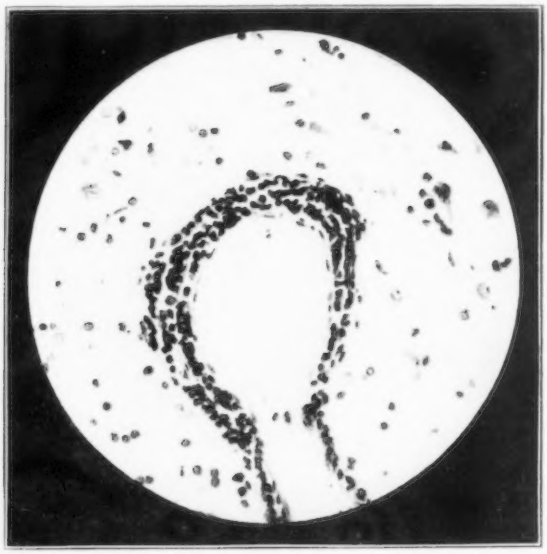

FIG. 25.—Venule from the cortex of a case of general paralysis of the insane. Note the high degree of adventitial proliferation; the intima is normal.

putable evidence in favour of the lymphogenous genesis. This latter view is upheld on clinical and experimental grounds by both Wickmann [43] and Römer [37], and with them we agree. The localization and morphology of the lesions and the continuity of extension are characteristic of lymphogenous infections, a continuity which varies naturally, and attains its maximum in the acute ascending paralysis of Landry.

There is one important feature in connexion with the question of lymphogenous propagation and extension to which Homén [13] has drawn attention—viz., that the posterior root ganglia act as traps or

filters, and form a kind of barrier against the further centripetal passage of organisms. This observation, although difficult to explain at present, would seem to be of special significance, as in all our experiments dealing with lymphogenous infection we have found a large collection of reaction cells and hæmorrhage at the proximal pole of the ganglion. It may be that this special reaction indicates the existence of some defence mechanism against the further central extension of toxi-infection, and that an additional factor is introduced by a local anatomical structure. It is of interest to note in this connexion that an analogous though more intense lesion is found in the ganglion in herpes zoster, and we would suggest that this disease also falls into the lymphogenous group, for we have observed the typical clinical appearances and pathological lesions of zoster to follow an empyema accompanied by ascending inflammation of the intercostal nerves. It is not improbable, therefore, that Homén [13] is quite correct in calling the root ganglion a trap for noxious agents ascending in the lymph-stream of nerves; and if we accept that it is a defence mechanism, and herpes zoster an expression of arrested ascending lymphogenous infection, then the suggestion might be put forward that the exciting agent which is not trapped passes onwards to the spinal cord and causes meningo-myelitis in some form or other.

A consideration of the phenomena in the subacute non-systemic lesions of the cord such as occur with or without anæmia, Addison's disease, cancer cachexia, &c., shows that they must be included in the hæmatogenous category. There is an entire absence of the proliferative change in the adventitia of the veins and capillaries which characterizes the lymphogenous infections. The root entry zones in the posterior columns are, except perhaps in the latest stages of the affection, quite sound, while there is a marked sclerosis around the postero-median septum. The nerve-cells in the grey matter maintain their integrity. The morbid picture is degenerative, not inflammatory; in type and in the zones affected it corresponds with what is found in experimental hæmatogenous intoxication.

In describing the lesions produced in our experiments we have indicated that the cellular elements present in the inflammatory reactions have, under varying conditions, exhibited markedly different characteristics. On the other hand we have found that where the conditions have been as nearly identical as possible similar appearances

have been produced. If the extremes in the series—the swollen nuclei and the plasma-cells in the walls of the veins and capillaries in the sub-acute cases, and the accumulations of cells indicative of an acute lesion or of destruction of nerve tissues in the other cases—had alone been considered, we might have been led to describe these conditions as distinct classes or varieties of reaction; but, seeing that it has been possible to observe a series of intermediate stages, extending from one extreme to the other, such a division was evidently not justifiable. Hitherto such an arbitrary separation has been attempted under the terms hæmorrhagic, interstitial, and parenchymatous inflammation. Possibly from the point of view of the clinician this division was of use, and especially so seeing that the pathology of inflammatory processes in the nervous system was not established on a scientific basis. But since the pathology of these conditions and the mechanism of their production have been more thoroughly investigated such a classification can no longer be admitted. Still, although so much work has been done and many valuable data have been collected, the results have been somewhat contradictory and a certain amount of confusion exists even now. It has been shown, however, by the investigations into the characters, the origin, and the significance of the various types of cells, that inflammatory processes in the nervous system must be considered as a whole; and only by considering the etiology and the mechanism of production of these processes together with the results revealed by the microscope will it be possible to explain the various morbid conditions.

The experiments which we have carried out may be divided into two classes, viz., firstly, those in which there was no escape of organisms from the capsule and in which, therefore, the results must be regarded as the effect of the action of a toxin on the tissues; and secondly, those in which the capsule had leaked or in some cases burst and there followed a growth of organisms outside which produced a much more intense reaction. But although we have divided the experiments into these two classes we hope to show that the differences in the results are more a matter of degree than of kind.

In the series in which there had been no escape of organisms from the capsules, the chief type of reaction cell present was the plasma-cell. Attention has been directed to the characters and origin of these cells since the appearance of Unna's work on their existence in granulation tumours of the skin and more especially since the work of Marschalkó [20] in 1895. Unna [41] based his definition of these cells on their

staining properties, Marschalkó [20] relied on their morphological characters. But while the description of Marschalkó for the fully developed cells is still retained it has become recognized that their form and staining capacity may vary considerably under different conditions. Nissl [24], referring to the early stages of the overgrowth of the tissues of the walls of the vessels, said that "quite small forms of plasma-cells may be seen with a small cell body which stains much more deeply than is usual in these cells." Degenerative phases also have been described. In this phase they sometimes resemble reticulate cells (Unna [41]), or they may be vacuolated, or they may show solution (Herbert) or hyaline degeneration of their protoplasm (Joannovics [16]); some authorities have seem them loaded with pigment. The recognition of these forms is important and materially assists in the task of determining the origin of these cells and their relation to the cells amongst which they are found.

The question of the origin of plasma-cells has given rise to endless discussion. Unna [41] considered that they were derived from connective tissue cells; Marschalkó [20], on the other hand, traced them from the lymphocytes of the blood, and chiefly from the veins. This view was held for a long time and has been strongly supported by Nissl [24]. Nissl has stated that he is firmly convinced that plasma-cells are exclusively of hæmatogenous origin, and that all the stages between the lymphocyte within the blood-vessels and the plasma-cells in the sheath of the vessels can be traced. But when speaking of their appearance in granulation tissue he admitted that intermediate forms between Unna's plasma-cells and connective tissue cells, and also between Unna's plasma-cells and lymphocyte-like elements, existed. In another paragraph he stated that Marschalkó had observed cells with morphological characters similar to those of his plasma-cells in inflammatory granulation tumours and that they were sharply distinguished from lymphocytes and other cells with basophile bodies; but he added, "the typical Marschalkó plasma-cell is not so absolutely distinctive that it can under all conditions be separated from the lymphocyte-like elements and connective tissue cells with basophile cell-body, and, further, intermediate stages occur between those forms of cells." Observations similar to these have led many investigators to speak of two varieties of plasma-cells: those of Unna—histogenous—and those of Marschalkó—hæmatogenous. Joannovics [16], in a paper published some years ago, said that plasma-cells, besides finding their origin from lymphocytes of the blood, could be derived also from the cells of

connective tissue under certain conditions. In a more recent paper he recognized a histogenous origin only and brought forward, amongst other evidence, the following reasons against the hæmatogenous theory: (1) Inflammatory tissues are invaded by leucocytes, but there is no increase of intravascular lymphocytes. (2) Schridde and he claim to have followed plasma-cells from the tissues into the blood-stream during digestion. (3) The presence of plasma-cells in normal tissues, when no relationship to lymphocytes can be traced, makes it difficult to admit their origin from the blood elements. Marchand also considered that certain adventitial cells possess the capacity of forming elements having the characters of lymphocytes and large mononuclear leucocytes, and he applied the term "lymphocytoid" to the cells formed outside the blood-stream; amongst them he included plasma-cells. The separation of the tissue lymphocytes from the hæmatogenous lymphocytes has been strongly supported by Pappenheim, who held the former to be the mother-cells of the plasma-cells. These tissue lymphocytes are now regarded as histogenous elements which have sprung from sessile perivascular cells, normal constituents in the walls of the vessels, under the influence of physiological and pathological stimuli, and from these tissue lymphocytes the plasma-cells are developed. Schmauss [38] also has spoken of the usually sessile elements of the vessels becoming wandering cells under suitable stimulation.

In our experiments the toxin derived from the capsule containing the organisms produced a reaction in the various tissues along the path by which it advanced towards the central nervous system. In the cases in which the capsule had not burst and there was no growth of organisms in the tissues, this reaction was most marked in the adventitial sheath of the veins and capillaries: the cells of this sheath were undergoing a very active proliferation and, as a result, collections of cells of various forms appeared. Most of the cells had a rounded shape; the nucleus was round or oval; it stained deeply and uniformly in some and in others the chromatin was arranged around the nuclear membrane. The quantity and the disposition of the protoplasm varied also. In some cases there was no protoplasm to be seen; in others a very thin layer surrounded the nucleus: in some, again, the protoplasm was separated from the nucleus by a clear space. Another phase was indicated in cells whose nucleus had become excentric with a clear space on its central side bounded peripherally by a layer of vaguely granular protoplasm. This series of cells demonstrates the intermediate stages in the development of the typical plasma-cell from the rounded

elements occurring amongst the proliferated cells of the adventitial sheath. In some areas the endothelial cells of the small veins and of the capillaries were swollen and irregular in shape; they projected into the lumen and, in some instances, were detached and lay free in it. In connexion with this it is interesting to point out that Beattie [5] has described a swelling of the intimal cells and their complete detachment from the walls of the vessels in omental inflammation. Adami [1] also has said that "the evidence accumulating of late years appears to point in one direction, namely, that the mononuclear cells seen within the vessels during the process of inflammation are of endothelial origin." Occasionally, in our experiments we have found many of these cells in veins partially thrombosed, but at the same time there was no special collection of them in the adventitial sheaths and they were not seen passing through the walls of the vessels. That thrombi can be formed in the vessels during the early stages of similar inflammatory processes has been demonstrated by Righetti [36] after injection of diphtheria toxin into the sub-dural space. It will be necessary, therefore, to bear these conditions in mind when discussing the origin of plasma-cells from mononucleated cells within the vessels. In the small veins and capillaries further from the source of the irritant, for example, in those situated near the central canal of the spinal cord, the sole reaction present was a slight swelling of the nuclei and an increased staining capacity of the cells of the intima.

But, besides the cells of the adventitial sheath, those of other tissues were reacting, especially at the level of the seat of the capsule. The cells of the epi- and perineurium in Series I, and of the dura mater and of the areolar tissue outside it in Series II, were proliferating, and in the collections of cells thus produced definite plasma-cells and also examples of the intermediate forms referred to were numerous. The nuclei and cell-body of these plasma-cells in the dense tissues were narrow and elongated, and the latter stained deeply with the toluidin and pyronin-methyl-green methods; the intermediate forms were shown by the nuclei becoming more rounded and by a halo appearing on one side of it. In the loose areolar tissue various forms from the small round nucleus to the typical plasma-cell lay along the trabeculæ.

The evidence derived from these experiments, therefore, suggests that plasma-cells may spring from the cells of the connective tissues as well as from the adventitial sheath of the vessels. Catòla [8] has found plasma-cells in the liver in cases of general paralysis, not around the vessels but amongst the cells of the perilobular connective tissue

and around the biliary canals—in fact, in regions where the connective tissue was proliferating. The fusiform cells of this tissue were described as being strongly basophile: their protoplasm increased gradually in quantity and they assumed the morphological characters of plasma-cells. A similar appearance of these cells derived from connective tissue has been demonstrated by Pappadia [33] in the wall of a cysticercus cyst in the brain. Here, also, the fusiform fibroblasts swelled up and exhibited a basophile protoplasm; they gradually became polygonal and rounded in the outer layers of the cyst wall and acquired the characters of typical plasma-cells.

The conditions found by these investigators led them to suggest that these cells may spring from the cells of the connective tissues; the results of our experiments and the examination of tissues taken from clinical cases, e.g., the fibrous sheath of a lymphatic gland invaded by a metastatic growth from a malignant tumour of the lower jaw, have demonstrated that in certain instances such an origin must be admitted. At the same time there can be no doubt that in our experiments the great majority of the plasma-cells sprang from the proliferated cells of the adventitial sheath.

In the experiments in which the capsules had burst and the organisms had grown amongst the tissues another type of cell, corresponding to the polyblast of Wickmann, was the most prominent feature in the sections examined. In his cases of acute poliomyelitis, Wickmann [43] found the walls of the vessels occupied by large cells with a rounded or oval nucleus, often indented on one side; the cell-body was sometimes clear, but in many instances it contained a few deeply stained masses irregularly distributed. Frequently, the nucleus was so much indented and its form was so irregular, that it resembled that of a polymorphonuclear leucocyte; the chromatin was collected into a few small granules united by a reticulum. By many observers these cells have been regarded as polymorphonuclear leucocytes, but Wickmann [43] maintains that this view is not correct. Most of the infiltration into the pia mater is undoubtedly of lymphocytic origin, i.e., the cells have sprung from the wandering lymphocytes of the adventitial sheath of the vessels, and Wickmann argued that a similar derivation must be admitted for the cells found in the spinal cord. He recognized many intermediate forms between these cells and the lymphocytes. The following arguments were adduced against the leucocytes being the progenitors of the polyblasts. It was admitted that the nucleus of the polyblast might be so much lobed as to resemble the nucleus of

the polymorphonuclear leucocyte, but it possesses granules of chromatin united by a reticulum which is not seen in the leucocyte; and in tissues fixed in alcohol the cell-body of the polyblast is stained by the pyronin-methyl-green method, while that of the leucocyte is not; and by other suitable staining neutrophile granules can be demonstrated in the leucocyte which are absent from the body of the polyblast. Wickmann [43] concluded that, in his cases, the polyblasts sprang from the wandering lymphocyte and that the hæmatogenous leucocyte did not participate in their formation. He admitted that some of the small neuroglia cells offered appearances difficult to distinguish from the polyblasts, but the facts that these cells were found in the pia mater where there are no neuroglial elements, and in the sheaths of the vessels where they were obviously derived from the adventitial cells, are against such an origin. Moreover, in our cases, although a consideration of the small neuroglia cells might leave one in doubt, yet observation of the whole reaction of the neuroglial elements made it certain that the polyblasts did not owe their origin to them.

In our experiments the polyblast type of cell was seen best in the reaction in the pia mater and in the walls of the vessels passing from it into the spinal cord, in those cases in which the capsules had burst and the organisms could be followed along the intercostal nerves to the dura mater. In this region, where it was obvious that the potency and quantity of the irritant was much greater, all the cells of the pia mater and the endothelial and adventitial elements of the vessels were actively proliferating and the cells arising from this reaction were of the polyblast type. But at the site of the capsule which had not leaked some similar cells with pale nuclei, oval in shape, regular in outline, or indented on one side, were present amongst a far greater number of round, darkly stained nuclei and plasma-cells. This was the area of greatest intensity of reaction in this series, but it was not so acute as in the series with the burst capsules. It was easier, therefore, to follow the intermediate stages between the cells of the connective tissues and those of the walls of the vessels and the polyblasts. The polyblast, as well as the plasma-cell, is therefore of histogenous and not of hæmatogenous origin.

But besides the polyblasts in the areas of acute reaction there appeared around the capsule bands of fibroblasts, fusiform cells with an elongated, pale nucleus and a greatly increased quantity of basophile protoplasm which did not generally surround the nucleus but was collected at the poles. In some cells, however, the protoplasm encircled

the nucleus, and in others this was placed excentrically. Intermediate forms between the elongated fusiform cells and the rounded cells were evident. These bands of cells in parallel rows were present in all the experiments, but in much greater numbers when the capsule had burst.

With regard to the compound granular corpuscles, Gitterzellen (Nissl [24]), Körnchenzellen (Friedmann [11]), Abraumzellen (Merzbacher), a similar divergence of opinion has existed. Friedmann [11] divided these cells into two groups, granulo-adipose cells and epithelioid cells. The former he derived from white blood corpuscles and the latter from neuroglia chiefly, but also from adventitial cells. Schmaus [38] has admitted a double origin in foci of softening—in the early stages from polymorphonuclear leucocytes; later another type of cell, corresponding to the epithelioid cells, appeared. Of the origin of this type he was uncertain, but he thought they sprang from adventitial and endothelial cells. Merzbacher has called these cells Abraumzellen, indicating their function thereby; he traced them from adventitial cells and from the neuroglia. Nissl [24] has stated that not all the cells which contained fat were compound granular cells and he limited the term to those which acted as phagocytes; these he traced from the adventitial and endothelial cells. Schroeder found these cells in a focus in which there was some destruction of nerve-fibres but no proliferation of the elements of the vessel walls, and he concluded they were derived from the neuroglia cells. Bonfiglio [6], from his experiments, decided they had a dual origin, from the cells of the vessel walls and from the neuroglia.

It will be remembered that in the lateral columns of the spinal cord when the growth of organisms had spread along the intercostal nerves to the dura mater, a considerable collection of cells had appeared which offered some definite peculiarities of structure. The nucleus was deeply stained and often situated at the side of the cell; but the chief peculiarity lay in the formation of a reticulum in the cell-body (fig. 20). In many cells the spaces of this reticulum were unoccupied and gave the appearance of vacuoles, but in others they were filled by a material which was faintly stained. Cells with a reticulum in the cell-body occurred also in the epidural tissue—i.e., in the region of the most intense reaction—in the cases in which the capsules had not burst. Here they were mixed with a large number of polyblasts and plasma-cells, in their adult and intermediate stages, and with a form of cell which has been spoken of by Friedmann [11] as the epithelioid cell. In these situations the appearances suggest that these reticular com-

pound granular cells have sprung from the proliferated elements of the adventitial sheath of the vessels and of the connective tissue cells of the epidural sheath. But in the most recent series of experiments, in which the capsules had been placed in the peritoneal cavity and in which nutritive changes had occurred in the spinal cord, similar cells were met with in close relation with nerve-fibres undergoing degenerative changes. In these cases there was no reaction of the cells of the adventitial sheath, and it was evident the compound granular corpuscles present were derived from the neuroglia cells.

An examination of the results of many investigations regarding the origin of the types of cells referred to in this paper, and of the phenomena observed in the experiments in which we have induced inflammatory processes of varying degrees in the nervous system, provides conclusive evidence that the cells of reaction against an irritant are derived from the cells of the tissues with which the irritant comes into contact; in other words, all these varieties of cells—plasma-cells, polyblasts, fibroblasts, epithelioid cells, and Körnchenzellen—are of histogenous and not of hæmatogenous origin.

The fact that all these forms of cells of reaction have been traced from a common source suggests that there must be some principle underlying these processes which, if discovered, would prove that they are not so independent of each other as they have often been assumed to be, and would clear away much of the confusion at present obscuring the question. One of the chief difficulties has been the insistence on the use of the word "typical." We constantly see reference made to the "typical" plasma-cell, to the "typical" polyblast, or to the "typical" Körnchenzell, and by many the cell which was not a "typical" cell of some sort has been left out of consideration. Bonfiglio [6] criticized the statement of Nissl [24] that too much importance was not to be attached to the presence of intermediate forms. Such a statement might be accepted when dealing with isolated cells, or with cells in small numbers, but when the intermediate forms exist in large numbers they should not be ignored. Another difficulty has been that the investigations have not been carried out on sufficiently broad lines; that which has been simply one stage in a complex inflammatory process has been examined without due attention being given to the conditions under which the process arose and to the earlier stages through which it may have passed. Hints of the necessity of looking beyond the mere type of cell have been made by several observers; for instance, Wickmann [43] has suggested that the nature of the infiltrating

cells depends on the irritating agent and not on the localization; and Bonfiglio [6] expressed the opinion that in different pathological conditions these elements may have a varying origin. There can be no doubt that in order to understand the significance of a reaction occurring in the nervous system it is necessary to consider the cause of the inflammatory process, its intensity and the length of time it has acted, together with the morphological form of the cells infiltrating the tissues.

A more comprehensive communication on this subject has been published by Friedmann [11], in which he has given the results of his investigations regarding the reactions which accompanied different degrees of irritation in the nervous system. He started with a simple form of morbid change, viz., hyperæmia, and found that the vessels and the lymph spaces in their sheaths were dilated, and that regressive changes had occurred in the elements forming the vessel walls. When a hæmorrhage had taken place amongst the nerve tissues, a definite reaction followed. The blood soon disappeared, chiefly in the lymph spaces of the vessels in the neighbourhood, and at the edge of the area containing the hæmorrhage a cyst wall had formed, consisting largely in dense connective tissue fibrils, vessels and cells. Outside this, in the tissues limiting the softened area there was a looser cicatricial tissue infiltrated by a large number of Körnchenzellen. In cases of thrombosis or embolism there followed a complete anæmia and an intense œdema in the centre of the focus. In a short time this centre was occupied by the detritus of broken-down nerve-cells and fibres, and in this were many Körnchenzellen. Experiment proved that these cells appeared on the second day and that their numbers increased during the following days. Then later the fibrous organization and sclerosis characteristic of encephalomalacia followed. These were the constant results after simple destruction of nerve tissues by vascular lesions.

Then in his experimental work he showed that slight aseptic wounds of the brain produced a central necrosis immediately surrounded by a necrobiotic area containing many Körnchenzellen and a peripheral zone with round cells, new vessels, and a proliferation of the fixed tissue elements, leading to a sclerosis. With a more intense irritation, such as the application of corroding agents to the brain, the process was more active. At once, around the necrosed, corroded area, there was a condition of irritation of the vessels with hyperæmia, extravasation of blood and emigration of round cells. By the third or fourth day the neuroglia cells were swollen and Körnchenzellen were present; and from the fifth day a breaking down of the nerve tissues was observed

and also large collections of epithelioid cells and Körnchenzellen. The vessels were thickened by proliferation of the endothelial cells, new vessels were formed, and organization followed. Here again there was a destruction of nerve tissues, but the cause had acted also as an irritant to the mesodermal tissues.

In still more acute cases, the result of a meningitis or an invasion by the influenza bacillus, the hyperæmia, with or without a softening, was followed by an active proliferation of the fixed tissue elements. From this proliferation there appeared Körnchenzellen and other large, round cells, the epithelioid cells. These last were often not limited to the sheaths of the vessels but infiltrated the tissues, without, however, any real softening being present. Much new vessel formation occurred. The termination of the acute process was either a primary organization and cicatrix—and this was the result in the corroding experiments—or, as happened in the encephalitic cases, the young cells formed a protoplasmic network whose meshes were occupied by round cells, and then later this contracted and formed a cicatrix. In other areas there was a large collection of fibroblasts, or, where a central necrosis had occurred, the usual cyst wall was found. In cases of abscess in the central nervous system there was a migration of leucocytes in the first few hours and the neuroglia cells were swollen. On the third day the nerve tissues were breaking down and Körnchenzellen were as numerous as the leucocytes. By the tenth day the area of infection was surrounded by a membrane consisting in (1) a layer with round cells, new blood-vessels, Körnchenzellen and disintegrating nerve tissue; (2) a layer with many vessels and fibroblasts forming a granulation tissue; (3) a layer in which the nerve tissues, although injured, were still preserved; the walls of the vessels were infiltrated, and the neuroglia cells were reacting. Friedmann [11] from this work arrived at the following conclusions:—

(1) All the different forms of reaction can be produced by the same agent or by any sufficiently strong stimulus, whether it be that which causes a meningitis or whether it be an embolism, an aseptic wound, an exogenous corroding agent or excessive heat.

(2) The whole complex series of changes from the small round cell infiltration, the intense inflammatory reaction with the giant cells and large cell proliferation, to the softening with "Körnchenzellen," may be present in one and the same case.

(3) The more intense inflammations progress by steps, and these steps correspond to those pictures of the morbid process which we have

been accustomed to regard as separate forms of encephalitis, hæmorrhagic, parenchymatous or hyperplastic.

This work is of the greatest importance in that it shows that although the inflammatory process under different conditions is exceedingly complex, there are certain principles underlying it which enable us to recognize in it different degrees of one process rather than several independent series of reactions. It demonstrates that not the particular kind of cause, but its intensity and the length of time it acts on the tissues, are the essential factors in determining the results. The initial stage may be a gross destruction of nerve tissue, and this will be followed by a reaction whose function it is to remove the débris, as in a case of hæmorrhage, thrombosis, or embolism; or it may combine a condition of irritation of the mesodermal tissues simultaneously with that of destruction, as in the action of corroding agents; or it may exhibit at first the phenomena of irritation induced by bacilli or their toxins, and the destruction of the nerve tissues will occur later. And, as Friedmann [11] has shown, the character of the reaction will change from day to day in the course of the process, especially when the irritation is the first result and the destruction follows.

Now, although the initial stages may vary so much, the final stage, following the destruction of the nerve tissues, presents fairly uniform characters; but here also the question of degree again arises. The necessity of separating these final from the earlier stages has been pointed out by Schmaus [38]. He admitted the continuity of the stages in the inflammatory processes occurring in the nervous system, but indicated that not all are the direct result of the action of the irritant. In some acute processes, where the irritant acts for a short time only, a slight parenchymatous degeneration is produced and the products of this degeneration may be disposed of by a reaction of the neuroglia without any infiltration of the tissues. But, if the breaking down of the tissues is more extensive, it is found that the reaction is more complicated. Besides the neuroglial overgrowth there is a large collection of phagocytic wandering cells. Again, the inflammatory process may be so acute that it affects not only the nerve-cells and fibres, but leads to a softening of all the tissues in the area attacked. This, at first sight, offers a very different picture to that which characterizes an ordinary simple softening. It is generally considered that a simple softening is distinguished by the presence of detritus and Körnchenzellen; but if the area of softening produced by an embolism be examined within a few hours of the blockage of the vessel, it will be found that there is

a swelling of the tissues, and the process goes on to the breaking down of the various elements; it is a liquefactive process, but it is also inflammatory, because it is accompanied by an emigration of leucocytes; only later do the larger phagocytic elements appear. In what is called an inflammatory softening the tissues become infiltrated with leucocytes, then break down, i.e., liquefy, and there remains a collection of degenerated tissue to be removed. Now the removal of this débris is accomplished by cells similar to those which act as phagocytes in the case of a simple softening, viz., by Körnchenzellen. But these cells are not the direct product of the action of the disease-producing agent, they are called forth by the presence of the débris of the tissue destroyed by the noxious agent. The Körnchenzellen are the type of cell which removes the products of degeneration, and they are recognized as the phagocytes of the central nervous system. Therefore, whatever may be the cause, the characters of the softening are fairly uniform, and are to be distinguished from those of the primary reaction which is the direct result of the action of the irritating agent. Schmaus [38] recognized, however, that there is no line of demarcation to be drawn between the two: the elements of the secondary process are intimately mixed with those of the primary reaction. Theoretically, the phases of absorption and organization may be sharply separated from the primary reaction, which includes the circulatory, regressive and progressive changes described by Schmaus [38] and others, but practically it is found that the elements capable of removing the débris are present at the same time as those of the primary reaction. Schmaus [38] stated that the separation offers least difficulty in the case of ischæmic degeneration of the nerve tissues following ligature of the aorta, but it is not possible in more chronic conditions. In the simultaneous degeneration of the parenchyma, the infiltration with wandering cells, and the overgrowth of the neuroglia, we see a temporary phase of a process which can end in sclerosis, but which during its course will present all the stages of inflammation. Besides, in toxi-infective myelitis the degeneration of the parenchyma may be the result of the action of the disease-producing agent, which is responsible also for the vessel changes, the exudation, the infiltration, and neuroglial overgrowth; or the infiltration and neuroglial overgrowth may be called forth by the presence of degenerated nerve tissues. Further, the thrombosis and embolism with the accompanying lymph stasis may be the direct result of the inflammatory irritant. In all these cases the different causes and signs of reaction will be so interwoven that it will be impossible to separate them sharply into primary and secondary processes.

With regard to the primary reaction, although its characters change from day to day and therefore the duration of the action of the irritant must be considered in judging of the appearances met with, yet it will be found that the type of the reaction will depend on the intensity and quantity of the noxious agent. We have referred already to the statement of Schmaus [38], that a slight amount of parenchymatous degeneration is followed by a simple reaction of the neuroglia cells; that in the early stages of a softening caused by an embolus there is a swelling of the tissues and a small emigration of leucocytes; and that with an acute inflammatory softening the tissues become infiltrated with leucocytes and there is an early reaction of the mesodermal tissues. The work of Nissl [24] also demonstrates the variation of the type of cells in reactions following different degrees of irritation. The injection of Indian ink into the subdural space led to the appearance of plasma-cells in the adventitial sheath of the vessels; after producing a localized necrosis of the brain by freezing he found an immense overgrowth of the cells of the intima and of the adventitial sheath of the vessels with the formation of fibroblasts; few plasma-cells were seen in the area of intense reaction, though they were numerous in the sheaths of the vessels in the surrounding tissues. Again, painting the meninges with chromic acid produced necrosis of the subjacent structures associated with the appearance of polymorphonuclear leucocytes in the focus of injury; this was encircled by a collection of fibroblasts, and very few plasma-cells were present except in the zone of tissue limiting the necrosed area. Here we see not only that slight irritations led to the development of plasma-cells, but also that with intense irritation, although the centre of reaction was occupied by leucocytes and fibroblasts, yet outside these where the irritation was less the plasma-cell was again the type of cell present.

Other observers have obtained similar results. Marschalkó [20] introduced small portions of sponge infected with cultures of gonococcus and weak tubercle bacilli into the peritoneal cavity and found later that there were no plasma-cells in the substance of the sponge, but many in the enclosing tissues. Reiz saw them in the brains of rabbits after introducing bits of elder pulp—in fact, the conditions produced by this method resembled those occurring in experimental tuberculosis of the brain. Joannovics [16] expressed his agreement with Marschalkó [20] that these cells are absent in the acute stages of inflammatory processes, but are present in subacute and chronic conditions of all organs: they appear in the recovery stage of acute inflammations. They are of

especial interest in gonorrhœa, which has a tendency to subacute and chronic forms; in gonorrhœal affections they are found in the submucous tissues more than near the surface. They are a prominent feature in all infective granulomata; in trichinosis; in the limiting wall of carcinomata. They are not found in the normal brain, but are present in many diseases of that organ, including lues cerebri, phosphorus poisoning, acute alcohol poisoning, status epilepticus and hydrophobia; they can, therefore, no longer be considered pathognomonic of general paralysis.

Now if we turn to the results of our experiments we find valuable support for the view that the character of the cellular reaction found in the nerves and in the spinal cord when the disease-producing agent approaches by the lymph-stream depends entirely on the potency of the irritant, and further, that many of the so-called varieties of cells have one and the same origin. When the capsule had not burst and the tissues were attacked by the toxin only, we found that the reaction produced was of the plasma-cell type, including under that term the numerous intermediate forms which have been described earlier in this paper. But in the other series in which the capsule had burst and the organisms had grown amongst the tissues, there was an altogether different picture. All the cells of the connective tissues and of the walls of the vessels exhibited an intense proliferation with the production of another predominating type of cell, the polyblast; there were also collections of Körnchenzellen showing various stages of development. It will be remembered that in the subacute series there were some polyblasts in the reaction outside the dura mater, i.e., quite close to the capsule. It was at this point that the results of the two series of experiments might be said to have met.

But seeing that in these two series of experiments a culture of the same organism was employed, and seeing also that the experiments were performed on members of the same species of animals, living under identical conditions, and that the animals lived about the same length of time after the operation, we consider that the difference in the reaction in the two series must be attributed to the difference in the intensity and quantity of the irritant. The reactions were produced in both instances by infected lymph which spread by the same path and therefore attacked the same cells. There can be no doubt that if the capsules in the second series of experiments had not burst the reaction would have been of the plasma-cell type, i.e., the type of cells characteristic of the subacute inflammations; but as the capsules had burst and

the organisms had grown amongst the tissues, the reaction was of the polyblast type, i.e., the type of the acute inflammations. Now these cells were the direct product of the action of the disease-producing agent and therefore the conditions corresponded to the primary inflammations of Schmaus. But we have shown already that there were small collections of Körnchenzellen, and it is certain that if the animals had lived a little longer and the nerve elements had broken down under the influence of the more prolonged action of the irritant, the tissues would have been infiltrated by these cells and the conditions would have corresponded to the secondary inflammations of Schmaus.

The distinction of the secondary from the primary reaction in the inflammatory process and the recognition that in the secondary reactions the Körnchenzellen have appeared, not as a direct result of the action of the irritant but because of the presence of the degenerated tissues, is a very important step in the elucidation of this question. Not only can a definite stage be recognized by the presence of these cells, but what is even more worthy of notice is that we have in the statements of Friedmann [11] and Schmaus [38] evidence that this type of cell is always associated with a particular function, and that the morphological form they assume is due to the fact that they have imbibed a certain amount of degenerated material. But not all the cells which take up the degenerated material possess the form of a typical Körnchenzell. Friedmann [11], when speaking of the difficulty of distinguishing epithelioid cells from Körnchenzellen, mentioned that the cytoplasm of the epithelioid cell may contain a relatively small amount of fat or of myelin: usually, however, the cell-body is clear and exhibits a network in its protoplasm, or it may be homogeneous. Various forms and sizes of the nucleus and of the cell-body are met with; there may be cells smaller than the typical Körnchenzell, in whose cytoplasm a little fat or myelin may be found, and there may be larger cells in which division often occurs. In these the nucleus is large, amœboid or irregular; or there may be several nuclei in one cell, and in that case the amount of protoplasm is relatively small and is distributed irregularly. We are therefore forced to recognize many forms which are not quite typical of the epithelioid cell or the Körnchenzell.

But it is not only in the removal of disintegrated tissue that the phagocytic action of the epithelioid cell is displayed. Homén [15] has shown that when micro-organisms have to be dealt with, polyblast and epithelioid cells predominate in the tissues. He demonstrated by experiment that injected tubercle bacilli are seen only occasionally in fibro-

blasts — and under that term he included adventitial cells — or in endothelial cells, and practically never in the neuroglia cells or their derivatives; on the other hand the polyblasts and epithelioid cells or epithelioid polyblasts were active phagocytes, and often contained several bacilli. Now this action in common exhibited by the two forms of cells demonstrates a close relationship between them. This has been recognized by Homén [15] and Wickmann [43], who consider that the epithelioid cells are derived from polyblasts. Fieandt [9] also has stated that epithelioid cells are polyblasts or are derived from them. In our acute series of experiments it was impossible to say where the polyblasts ended and the epithelioid cells began, and it must be remembered that in the acute conditions found in this series the nerve structures had been considerably affected by the irritant, so that products of degeneration were present as well as toxins. But polyblasts are cells which are characteristic of the primary stage of acute inflammatory processes, and they have been shown to be phagocytes of micro-organisms, while epithelioid cells are phagocytes of micro-organisms, and also of disintegrated products of nerve tissues. Further, the origin of the three forms of cells, polyblasts, epithelioid cells and Körnchenzellen has been traced from the cells of the connective tissues, and of the endothelial and adventitial layers of the walls of the vessels. They are therefore so intimately related that their division into three distinct types of cells is purely artificial and arbitrary; they should rather be regarded as three morphological forms of the same cell appearing under different conditions. Now in this connexion it will be remembered that in the subacute series the plasma-cell was the predominating cell, and it also was the offspring of the above-mentioned tissues. The irritant in this series was just strong enough to call forth cells possessing the characteristics of plasma-cells in some areas, while in regions far from the source of the toxin the reaction consisted in a swelling of the nuclei in the adventitial sheath of the vessels, and in a slight increase of the amount of the protoplasm around them: this was evidently the earliest stage of reaction. Outside the dura mater, near the seat of the capsule where the process in this series was most intense, we found some polyblasts and epithelioid cells, many of them containing several nuclei. These were scattered amongst a large collection of plasma-cells, most of which still retained the characters of these cells, while others exhibited various degrees of change which might be considered as intermediate forms between plasma-cells and epithelioid cells. This result, which we have spoken of already as the meeting point of the two

series of experiments, will explain the statement of Nissl [24] that the epithelioid cells were derived from plasma-cells.

The precise origin of the cells composing an inflammatory reaction is always a matter of great difficulty, and some points must remain obscure, but a consideration of the mechanism by which the inflammation is produced should prove of very great assistance especially in the case of lymphogenous infections. In experimental lymphogenous infection of the spinal cord of a subacute nature, in which all the inflammatory phenomena are extravascular and the path of the toxic lymph can be traced accurately, we find that besides the proliferation of the connective tissue in the meninges the only structures which react are the adventitial cells of the veins and capillaries and the neuroglia cells immediately in contact with them. The adventitia takes an extremely important part in the production of the cells of reaction; this is not surprising, seeing that the cerebrospinal lymph flows directly into its spaces. Hence when a toxin gains the central nervous system by the lymph path the cells of the adventitial sheath are the part of the vessel to be first attacked; and should the irritant be weak or permeate the tissues slowly no other phenomena need occur for some time. In more acute conditions, however, not only is there a more intense reaction in the tissues already mentioned, but the endothelial cells join in the process; and with a still greater degree of potency of the infection, intravascular changes, such as hæmorrhage and thrombosis, complicate the picture.

But besides the difference in intensity of the reaction in its primary stage the forms of the cells of reaction also vary. Thus it is that in our experiments we find changes ranging from simple swelling of the nuclei, together with a slight increase of the protoplasm around them, to fully formed plasma-cells and polyblasts; and as the process advances these cells often become epithelioid or reticulate in type, and by the imbibition of the products of degeneration, assume the characters of the compound granular corpuscles, which are such a constant feature of the secondary phases of inflammation. The entire reaction, therefore, although it presents several stages, must be recognized as one continuous process.

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# UNUSUAL TYPE OF HEREDITARY DISEASE OF THE NERVOUS SYSTEM (PELIZÆUS - MERZBACHER), APLASIA AXIALIS EXTRA-CORTICALIS CONGENITA.

BY FREDERICK E. BATTEN, M.D., AND DOUGLAS WILKINSON, M.D.

## Introduction.

The disease about to be described is a familial and hereditary one, having its onset in the first three months of life, even if it is not actually congenital. It presents symptoms which in many respects are similar to those seen in cases of disseminated sclerosis, cerebellar disease, and in its later stages to Friedreich's disease. It is very slowly, if at all, progressive, affects chiefly males, and is transmitted by healthy females. In the family here described males only are affected. It corresponds to none of the commonly recognized types of familial affection, but the symptomatology so closely resembles that presented by the family recorded by Pelizæus and Merzbacher, that we believe the disease to be of the same nature, although no pathological examination has been made in any member of the family here described. The cases published by Nolan also resemble these cases clinically, but no pathological examination has been made.

When the children were first seen we were inclined to associate the condition with some congenital defect in the development of the cerebellum, such as occurs in litters of cats and puppies, and have been recorded by Herringham, Andrewes, Risien Russell, and others, but after studying the pathological anatomy as put forward in Merzbacher's excellent paper, we have come to the conclusion that our cases probably belong to that group.

## Clinical and Familial Features.

The family history is best studied from the following tree, the usual signs being used. The numbers below the affected individuals refer to the number of the case in the text.

The family first came under notice when two boys, aged 4 and 2, were admitted into the Hospital for Sick Children, Great Ormond

Street, in November, 1913. The family history as obtained from their mother was as follows:—

W. J. W., father of Cases 3 and 4 and grandfather of Cases 1 and 2, appears to have been normal. He married, had twelve children, and died of phthisis in 1905. As he was born in Yorkshire his wife does not know any of his family, but to the best of her knowledge they are all dead. Her family are all quite normal, and since the death of her first husband (W. J. W.) she has married again and has given birth to a normal son.

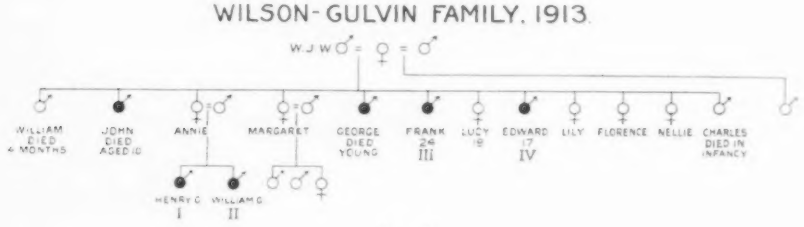


FIG. 1.

DETAILS OF THE TWELVE CHILDREN.

(1) William, died at the age of 4 months of convulsions.

(2) John, lived to the age of 10; he could not sit up or talk properly, was subject to fits, and died of a brain abscess (?).

(3) Annie, is the mother of Cases 1 and 2; she is quite normal, and appears to be of more than usual intelligence.

(4) Margaret, is well and married; she has two boys and a girl who are quite normal.

(5) George, died as a baby; he is thought to have been like the patients.

(6) Frank (Case 3).

(7) Lucy, is well, aged 19; she is not married.

(8) Edward (Case 4).

(9) Lily, died as an infant of pneumonia.

(10) Florence, is well and unmarried.

(11) Nellie, is well and unmarried.

(12) Charles, died as an infant; nothing is known of his condition.

In addition to the above children there were three or four miscarriages.

CASES.

*Case* I.—Henry G., aged 3 years 9 months. Was a full-time child, breast-fed for nine months. He never had any acute illness or fits. He is rather small for his age. He is generally a quiet child, but when he does cry he is extremely noisy and persistent. He does not appear to take much interest in anything, and cannot talk. The mother says that while he cannot say any words clearly except "Mum" and "Dad," yet he makes sounds which she can understand. He will take hold of a piece of paper with either hand, and in so doing shows a slow ataxic tremor of the whole arm.

*Eyes.*—There is a constant concomitant wheel nystagmus, which is not increased by looking in any direction. In this movement the pupils describe an ellipse with the long axis horizontal. There is no rotation of the eyes on their horizontal axes. The pupils are equal, regular in outline, central, react to light, and appear to react to accommodation. Vision seems good, and the fundi appear normal.

FIG. 2 shows the appearance of one member of the second family. The boy restrains movements of the hands by clasping them together and pressing them against the trunk. Note the normal appearance of the shape of the forehead.

*Motor.*—While the child can move all his limbs and also the head from side to side, he cannot sit up, nor can he support the head when sat up. When placed in the sitting position there is a slow nodding tremor of the head which falls forward on to the chest, and in this position the nystagmus becomes slightly more marked. There is some ataxia of the legs, but owing to their greater weakness it is not so marked as that in the arms. There is a slight degree of hypotonia in both legs and arms.

*Reflexes.*—The knee- and ankle-jerks are present. The plantar response is of an extensor type. The superficial abdominal reflexes cannot be obtained.

There is no abnormality in the contour of the head or vertebral column. The

mouth is rather crowded with poorly developed teeth, and the palate is rather arched. Swallowing is quite normal, but the boy cannot feed himself. The chest is poorly formed, there being well marked lateral grooves and depression of the lower end of the sternum. There is generalized bronchitis present, with a loose and frequent cough, but no expectoration. On the skin of the chest and arms there are several patches of lupus, and there is a dactylitis of the first phalanx of the little finger of the left hand, which is possibly tuberculous. At night the child frequently has profuse sweats. The boy gives no indication of his desire to pass urine or fæces.

*Case* 2.—William G., aged 2 years 1 month, was born at full time, and was breast-fed for a year. Neither in this case nor in that of his elder brother was labour difficult or tedious. He has always been "delicate," but has never had any illness, convulsion, or fit. While he is a well grown child his legs appear to be less well developed than his arms. He is a restless and irritable child, often moving the head from side to side and crying loudly and persistently. He appears to take very little interest in his surroundings, but a piece of paper attracts him, and he will grasp it with the left hand, but then only moves it about in a purposeless manner, showing a slow ataxic tremor of the arms as he moves.

*Eyes.*—The eyes are in every respect exactly similar to those of Case 1.

*Motor.*—The child can move all his limbs, but the legs are weak. He prefers the left hand to the right, and appears unable to grasp with the latter. He cannot sit up unsupported, nor can he support the head when sat up. On voluntary movement he shows the same slow tremor that is present in Case 1. There is slight general hypotonia. In addition to the tremor the child shows curious, almost athetoid, movements of the fingers before grasping an object.

*Reflexes.*—The knee-jerks are present, but no ankle-jerks can be obtained. The plantar responses are of the infantile extensor type. The superficial abdominal reflexes cannot be elicited.

There is no abnormality in the contour of the skull or vertebral column. The teeth are only partially erupted (there are eight in the upper and four in the lower jaw) and are poorly formed. The palate is very arched. Swallowing is performed quite normally. The child has to be fed.

The similarity of these two cases is very striking; their expression, attitude, reflexes, &c., are in almost every particular identical, and with the exception of the lupus and a slight difference in size it would have been difficult to distinguish between them. Both showed a slight relative under-development of the lower part of the body, the legs being disproportionately small.

*Case* 3.—Frank W., aged 24, inmate of B—— Asylum, uncle of the above, has been affected with the disease from which he suffers from birth, and his condition is now the same as it was when he entered the asylum some years ago.

He is friendly, and appeared rather pleased to be examined, smiling most of the time. While he understands what is said to him well enough to carry out simple orders—he picked up a penny from the counterpane, transferred it to the other hand, and finally handed it to the owner—he is obviously impaired mentally. He cannot feed himself owing to his tremor.

*Speech.*—He is said never to talk spontaneously, but attempts to answer questions quite willingly. His articulation is so imperfect that little of what he says can be understood by those unaccustomed to his speech.

FIG. 3.

FIG. 4.

Figs. 3 and 4 show the appearance of F. W., aged 24. They show the well-developed arms, the wasted legs and the position of the feet.

The constant movement and overaction is in part shown in fig. 3, by the position of the right arm, and in fig. 4 by the facial expression.

*Eyes.*—The pupils are regular, react to light and accommodation. There is no strabismus, nor any apparent ocular muscle weakness. There is a constant concomitant, wheel nystagmus, which is unaltered by any movement of the eyes. There is no rotation of the eyeballs in this nystagmus. Vision appears to be good and the fundus normal.

Hearing is good.

The tongue is protruded rather jerkily, but appears normal otherwise. Sensation does not appear in any way impaired.

*Motor.*—While the arms and chest are well developed, and even surprisingly muscular, the legs are wasted and thin, especially below the knees. The patient uses the arms to turn over in bed, &c. He cannot stand or sit up in bed unassisted. The legs are kept constantly flexed at the knees and hips, and there is a considerable degree of adductor spasm. The feet are flattened with a tendency to eversion of the soles and slight foot drop. Movement of the legs is very feeble. On performing any movement a slow, wavy tremor is at once apparent; this is best seen on sitting up, when, in the effort to support himself, rotary and nodding movements of the head become very marked. There is also a well-marked slow tremor of the arms on attempting any movement. A tendency to hypotonia is shown by the fact that the feet can easily be flexed to less than a right angle, but on the other hand the arms are held rather stiffly and there is a slight delay in relaxing the grip.

*Reflexes.*—The knee-jerks are present, the right more marked than the left. There is bilateral ankle-clonus. The deep reflexes are easily elicited in the arms. The superficial abdominal reflexes are absent. The plantar response is definitely extensor on the right, indefinite on the left. Sphincter control is good, but at night there is occasionally incontinence, probably because he fails to attract the attention of an attendant.

The skull is well formed, except that the occiput is rather flat: the circumference is 20 in., and from meatus over the vertex is nearly 15 in. There is a mid-dorsal scoliosis, the convexity to the right.

*Case* 4.—Edward W., aged 17, brother of the last case: inmate of S—— Workhouse Infirmary. He has been affected since birth, and so far as can be ascertained his condition has not altered.

He resembles his brother in appearance and disposition, but seems to be rather more intelligent. He is said to take considerable interest in the other members of the ward, and to talk to them. When he heard us mention his brother he said that Frank was like himself. He also carried out simple orders, picking up coins, &c. But he showed a very imperfect idea of their relative values, in that when offered a penny or a sixpence he preferred the penny.

Speech is very imperfect, but he attempts longer sentences, and is more easily understood than his brother. In speaking there is well-marked overaction of the facial muscles. One of his sentences was:—

"When you coomed in I weer go sleep."

*Eyes.*—The pupils are equal, and react normally to light and accommodation. There is no strabismus, but a wheel nystagmus identical with that shown by the other three cases. Vision appears good, and the fundi are normal.

Hearing is normal. The tongue appears normal, but there are jerky movements in protruding it. Sensation is not impaired. While he is fatter than Case 3, his muscular development in the arms is not nearly so good. He cannot sit up unassisted, or stand at all. The legs are kept flexed at the knees

and hips, but the flexion is less marked than in Frank. There is also some adductor spasm, but again less than in the brother. There is foot-drop, the feet being of the cavus shape, with some inversion of the anterior part of each. The legs are wasted, and in proportion to the arms very thin (this disproportionate thinness of the legs is more marked in Frank). The tremor which is evoked by any effort is the exact counterpart of that seen in Frank, but slightly more marked. Head nodding and rotation are also present. There is no hypotonia in this case.

*Reflexes.*—The superficial abdominal reflexes are absent, and the plantar response is definitely extensor on both sides. The knee-jerks are both exaggerated: the testing of the left elicits a knee-clonus. The ankle-jerks are present, and ankle-clonus can be obtained. He is occasionally incontinent at night, but otherwise has good sphincter control.

There is some flattening of the occiput, but otherwise the shape of the skull is normal. Circumference 20¼ in.; measurement from meatus to meatus, over the vertex 14 in. There is no spinal curvature in this case.

One of the most striking features in these cases is the similarity of their conditions. Edward and Frank resemble one another very closely indeed, as do Henry and William. All four patients show identical tremor and nystagmus, the latter of an unusual type; all have disproportionately small lower extremities, and none of them had superficial abdominal reflexes. Three of them showed some hypotonia, and all had extensor plantar responses. With regard to the mental condition in Cases 3 and 4, the defect seemed to us more apparent than real, and we were impressed with the idea that both are capable of considerable improvement if only they could be patiently and systematically taught.

The cases described by Pelizæus in 1885 closely resemble those of the family which we describe. In his family there were five cases in the children and grandchildren of one pair: three were dead and two were living at the time of the publication. All those affected were males, the disease being transmitted by unaffected females. The symptoms resemble those seen in disseminated sclerosis, tremor of the head, nystagmus, ataxia, slow speech, and spastic paralysis of the lower extremities.

There was also mental impairment, but it was more apparent than real. Sensation and control of the sphincters were normal.

The disease was present in earliest infancy, and was not progressive, the patients dying of some intercurrent disease between the ages of 20 and 30.

Merzbacher, in 1908, followed up this family, and found twelve instances of the disease, one of which he was able to investigate pathologically and report in a further paper entitled "Eine eigenartige

familiär-hereditäre Erkrankungsform (Aplasia axialis extracorticalis congenita)," published in 1910. He gives a family tree and further details with regard to this family which is republished here.

There are several discrepancies when compared with the tree originally published by Pelizæus, but the points that are brought out are: (1) that this disease has been observed in four generations; (2) that fourteen members of the family are known to be affected; (3) that it is always transmitted by healthy females; and (4) that males are more likely to be affected than females; only two of the fourteen individuals affected were females.

CONGENITAL FAMILIAL DISEASE, PELIZAEUS-MERZBACHER, APLASIA AXIALIS EXTRACORTICALIS CONGENITA

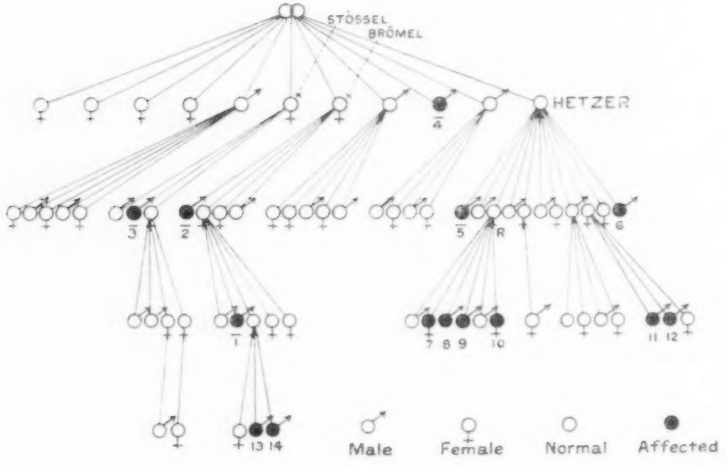


FIG. 5.

The clinical characters of the affection are given as follows:—

The disease begins in the first months of life; it makes rapid progress till the sixth year, then is more slowly progressive. When the disease is fully developed, it shows itself by nystagmus, slow speech, difficulty in the carrying out of motor impulses, disturbance of succession and co-ordination of movements, ataxia, intention tremor, "Mitbewegungen," masque-like facial expression, paresis of the back, pelvic

and abdominal muscles, paralysis and spastic contraction of the lower extremities, increase of the patella reflexes, Babinski response, loss of abdominal reflexes.

The following symptoms often accompany the above: trophic disturbance of the bones, vasomotor disturbance in the lower extremities, loss of mental capacity. The affected individuals may reach old age, and only die of some intercurrent disease.

The pathological condition was as follows:—

A normally convoluted brain, but small in all dimensions. The cerebellum, pons, and medulla appeared to be most affected in their size.

In the midline of the cerebrum the atrophy of the corpus callosum and fornix was most striking; so marked was this that on superficial inspection a defect of the corpus callosum was suspected. Sections through the brain showed that the smallness of the hemisphere was due to marked atrophy of the white substance alone. Corpus callosum and fornix were present, but very much atrophied; the anterior commissure was, on the other hand, well developed. The grey substance of the brain was of normal appearance.

In the section without further treatment one could observe isolated longish spots which lay in the white substance. These spots were shown by the Weigert-Pal method to be due to the fragmentation of the sheath of the medullated nerves.

In the central white matter of the various portions of the hemisphere and in some convolutions there were only small portions of normal fibre bundles remaining, and this gave the preparation a speckled appearance. These single remaining portions of the original tracts appear to be so disposed one to another that one island might be regarded as a continuation of its neighbour; thus a continuity of the medullary substance was rendered for the most part possible by the aid of the islands.

The most affected parts were the corona radiata and the corpus callosum, the great association systems were less affected. In the frontal, occipital, and temporal lobes and in the cerebellum the atrophy of the medullated fibres was most marked. Between the islands of the medullated fibres lay an unstained ground-substance. The collection of axis cylinders corresponded to the dissemination, size and extent of these medullated islands, and they too have suffered an apparent interruption in their continuity. The medullated fibres of the cortex and remaining grey substance showed no pathological change. The internal and external capsule, the crus, the pons, &c., were full of normal fibres.

The intact condition of certain bundles in the immediate neighbourhood of the cortex (Fibræ arcuatæ Meynert) was especially striking. The unstained ground-substance was composed of glia tissue. The structure conditions vary in different localities. Active proliferation of the glia was never present (except in the optic thalamus).

The destruction and absorption of other tissues has made the presence of the glia substance striking. It is believed that the unstained tissue contains very fine axis cylinders, and that the interruption of these was only apparent. Neither in the ganglion cells nor in the cortex were any pathological changes visible.

Sections of the medulla showed only a partial destruction of some system; no island formation was present. The cerebellar paths were most involved.

Merzbacher deals with a case recorded by Müller presenting somewhat similar symptoms, but differing pathologically, and concludes with a consideration of the whole question of hereditary degeneration.

In 1895 Nolan recorded three cases in a family whose genealogical tree is appended. In many ways these cases resembled those which we have described. They showed disease from birth, constant nystagmus, ataxia, and speech defect. One had increased knee-jerks, and bilateral ankle-clonus, but the other two showed loss of knee- and ankle-jerks. None of them could walk unaided, and two could not stand unassisted. They had no sphincter affection, no lightning pains, no foot deformity, and no sensory defect; differing from typical cases of Friedreich's disease in the early onset and slight increase of symptoms.

Their mental condition also was similar to that of the patients we describe, for, while they were backward, they showed none of the dirty habits, waywardness, or sexual depravity so often associated with congenital idiocy. They never spoke unless spoken to, but tried to answer questions, were of a cheerful aspect, and seemed pleased when noticed; in fact their defects seemed to lie chiefly in initiation and memory. In the following points, however, they differ from our cases; one patient was a female, and they all showed some indefinite wasting of the hands, flattening of thenar and hypothenar eminences, and some slight suggestion of "main en griffe." They were said to have shown some increase of symptoms, but their condition remained almost if not quite stationary after admission to the asylum.

Since these patients were recorded the two eldest members of the generation which produced them have married. Sarah has three children, of whom one, a daughter, is ataxic and "simple." David has

two sons who show speech defects. Unfortunately the details which can be obtained of these children are meagre.

Two of the patients described have since died of phthisis, and the third is at present suffering from the same disease. *Post-mortem* examinations were not permitted.

In conclusion, we are indebted to Dr. Cowan and Dr. Wolseley Lewis for their kindness in facilitating our access to two of the cases, and to Dr. Nolan for further details of his cases. It is hoped that some day we shall be able to confirm our view as to the nature of these cases by a pathological examination.

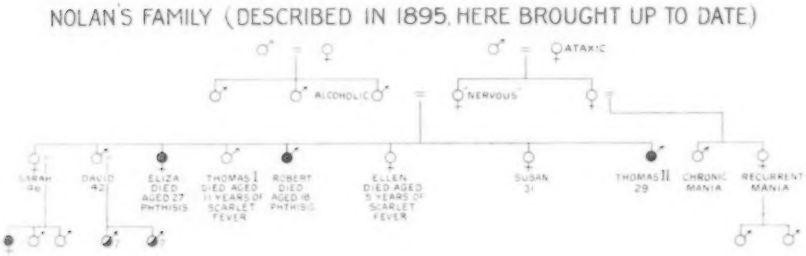


FIG. 6.

## SUMMARY.

A familial and hereditary disease, having symptoms resembling disseminated sclerosis, is described. Six males at least were affected in two generations. The subjects of this disease are almost always males, and the condition is transmitted by unaffected females. Those affected are either congenitally diseased or exhibit symptoms in the first months of life, the progress of the disease being very slow. They are mentally defective and ataxic, show nystagmus, speech defect, and defective development, with weakness and spasticity of the lower limbs. It is considered probable that these cases belong to the type of familial disease described by Pelizæus and Merzbacher under the title "aplasia axialis extracorticalis congenita."

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# AN ANATOMICO-PHYSIOLOGICAL STUDY OF THE POSTERIOR LONGITUDINAL BUNDLE IN ITS RELATION TO FORCED MOVEMENTS.

BY L. J. J. MUSKENS, M.D.

*Amsterdam.*

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## Introduction.

In previous investigations respecting the circus and rolling movements occurring in different species of vertebrates, I had observed the important part played by the posterior longitudinal bundle, when injured, in producing these phenomena [107,113]; I resolved therefore to make special experiments in this subject, and by means of the Probst "concealed needle" I made lesions in all directions, chiefly in cats, in the area between the nucleus of the abducens nerve and the posterior commissure. In each case the forced movements were noted, whether in the horizontal plane (circus movements) or in the plane vertical to the longitudinal axis of the animal (rolling movements). Forced movements were considered to be present, first, so long as the head and eyes remained deviated or so long as there was an inclination to go to one side, circus movements in a slight degree; and secondly, as long as there was an inclination to lie down or to fall to one side, which I look upon as a slight manifestation of rolling movement. The character of the movements and the direction of the locomotion which is the consequence of them are determined in accordance with the normal anatomical position of the animal, the normal posture being always reduced to that of the primary vertebrate exhibiting the simplest forced movements, for instance the fish.

A rolling movement exhibited by a patient, therefore, which commences with the turning of the chin to the left shoulder is, according to my nomenclature, a rolling towards the right, for, after reducing the posture and the movement to that of the primary vertebrate, this movement produces locomotion to the right from the original position of the animal.

The significance of the exact direction of the forced movement becomes at once apparent as soon as we begin to study the different pathological conditions of the ocular movements, conjugate deviation of head and eyes, and other neurological syndromes.

During my experiments, it was found necessary to draw a sharp distinction between forced movements in the horizontal plane, or circus movements, and those in the plane vertical to the longitudinal axis of the animal, or rolling movements. Various combinations of movements, however, were by no means infrequent, so that different animals appear in the table more than once; the character of the forced movements present being employed as a means of dividing them into groups.

Fig. 1*a*.

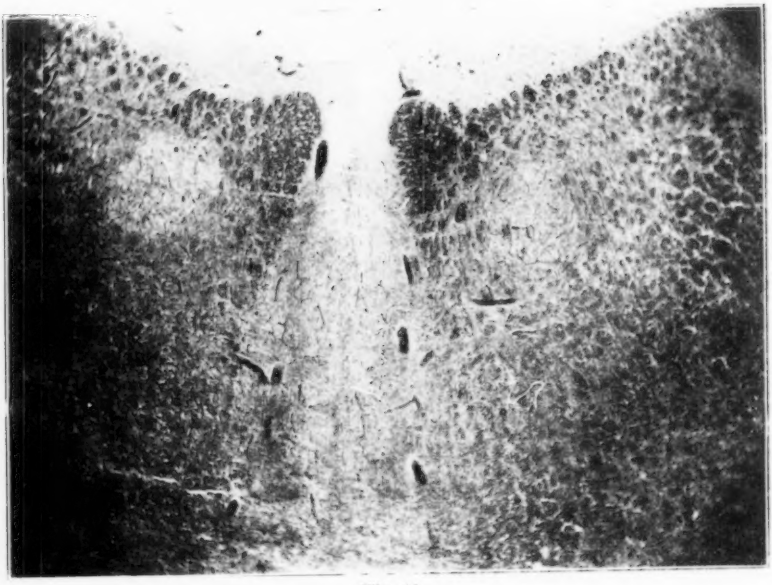

Fig. 1*b*.

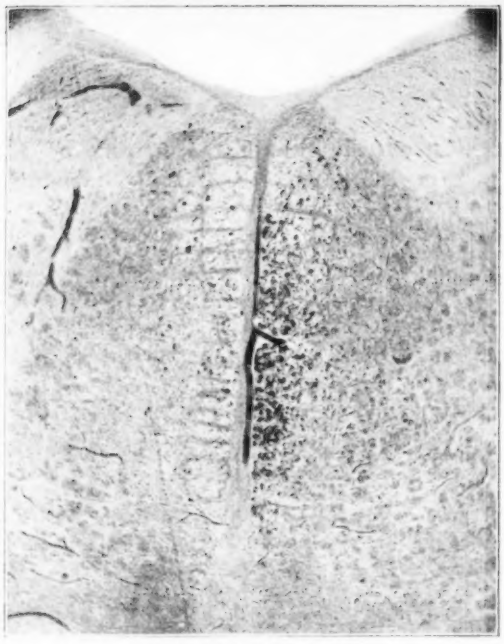

Fig. 1c.

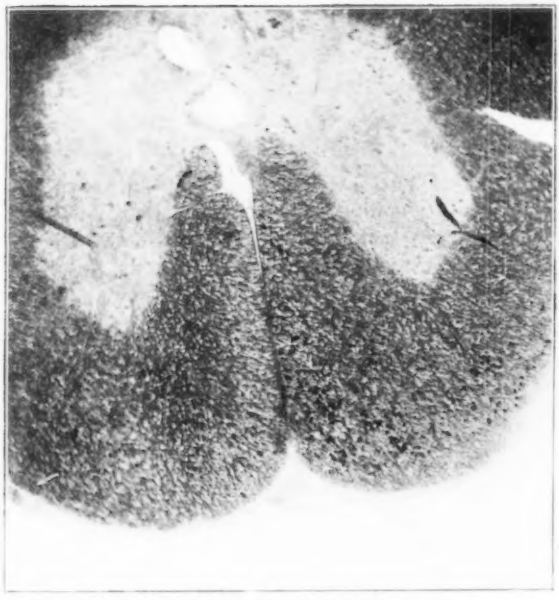

Fig. 1d.

FIGS. 1*a*, 1*b*, 1c, 1*d*.—Cross sections of cat No. 139.

Fig. 1*a*.—Stab through the posterior longitudinal fasciculus in the pontine region.
Fig. 1*b*.—Ascending degeneration in the region of nuc. tegmenti profundus.
Fig. 1*c*.—Descending degeneration in the medulla oblongata.
Fig. 1*d*.—Descending degeneration in the medulla spinalis dorsalis.

## Chapter I.—Secondary Vestibular Connexions and Forced Movements in the Horizontal Plane (Circus Movements).

### § 1.—*Lesion of the Mesial Part of the Posterior Longitudinal Bundle on one Side (Table I, Group 1, p. 376).*

In order to analyse the physiological functions of the different parts of the posterior longitudinal bundle, I endeavoured first to divide its mesial part on one side proximal to the sixth nucleus. In this I was successful in three animals (Nos. 91, 119 and 139); in one of these (No. 91) the lateral horn of the bundle was injured as well. Fig. 1 illustrates the lesion in the pons in one of these experiments and the resulting ascending and descending degenerations (cat No. 139).

In these animals circus movements towards the side opposite the lesion were observed for longer or shorter periods. This agrees with the results obtained by other investigators (*see* Table, Group 1) and is in harmony with the observations of Schiff and Probst that a hemisection of the pons causes circus movements to the intact side, but it would seem to show further that a total hemisection is not necessary in order to produce these movements, a lesion of the mesial part of the posterior longitudinal bundle being sufficient.

In all these cases there was a definite cerebro-petal degeneration in the posterior longitudinal bundle on the side of the lesion. This degeneration involved thick fibres which occupy a fixed position in the bundle, namely, in its mesial part and which correspond very closely in situation to the ascending bundle that, according to Thomas, Russell, Probst, Fraser, Lewandowsky, and van Gehuchten, is found degenerated after a lesion of Deiters' nucleus. Not infrequently some of the fibres of this latter bundle are found outside the actual area of the posterior longitudinal bundle and especially to its ventral side (Table I, No. 139 and No. 158). It ends close to the nucleus of the posterior commissure and appears to give off a number of fibres to the third nucleus. As far as I can judge from my own observations and those of others, these anatomical and physiological relationships are constant, and they suggest that we have to do here with an ascending vestibulo-mesencephalic bundle which controls circus movements to the opposite side.

A definite descending degeneration was present also in these animals. It was more pronounced on the side of the operation and could be followed on that side to the lumbo-sacral region in the antero-lateral column of the cord. On the other side, however, a few fibres were degenerated; these were situated more ventrally and laterally (Probst and van Gehuchten's reticulo-spinal bundle).

In the medulla, both these descending tracts leave their dorsal position in the posterior longitudinal bundle, and, according to Hösel, Probst, Winkler, Economo, and Karplus, take up a more ventral position. According to Wallenberg, the same change of position occurs in pigeons. Fraser observed it also in his experiments, but it must be borne in mind that he injured the posterior longitudinal bundle at the spot where the fibres enter it from Deiters' nucleus.

We shall have to consider presently the anatomical connexions of these descending fibres of the posterior longitudinal bundle. In order to simplify the narration of my results, however, I shall merely specify here what fibres were found degenerated. They were:—

(1) The descending fibres which, according to Held, Boyce, Redlich, van Gehuchten, Probst, Economo, and Karplus, degenerate on the side of the operation after lesion in the vicinity of the posterior commissure.

(2) Homolateral ponto-spinal or reticulo-spinal fibres which degenerate downwards after lesion of the substantia reticularis of the pons, as discovered by Probst, and confirmed by Lewandowsky and van Gehuchten.

(3) Heterolateral fibres constituting the crossed reticulo-spinal bundle which is found degenerated after lesion of the substantia reticularis of the pons (Kohnstamm, van Gehuchten).

### § 2.—*Lesion of the Posterior Longitudinal Bundle on both Sides* (*Table I, Group 2, p. 376*).

In a number of cats, I endeavoured to divide the mesial parts of both posterior longitudinal bundles and succeeded in doing so in four animals (Nos. 90, 92, 97, 114): in one of these (No. 114) they were divided in the neighbourhood of the posterior corpora quadrigemina, together with both lateral parts of the bundle (fig. 2); in another animal (No. 92) the mesial part of the posterior longitudinal bundle was cut on both sides, on the left somewhat frontally as compared with the right, and at the same time the lateral part also was divided on the left side (fig. 12). Three of these animals were incapable of locomotion; they could neither stand nor run, and their condition in many ways resembled that of rabbits during the first period after extirpation of both labyrinths (Winkler). There was conspicuous absence of lateral conjugate eye movements.[1]

[1] Observations on pathological cases with comparable symptoms and probably a similar lesion of the posterior longitudinal bundle have been recorded also by Parinaud, Priestley-Smith, Sauvineau Nieden, Long, Schöler, and Spiller.

In animal No. 90 both posterior longitudinal bundles were cut right across at the level of the exit of the trigeminal nerve except for the lateral part of the left bundle (figs. 11*a* and 11*b*, p. 387). In this case hæmorrhage took place exactly at the section of the left bundle, and this probably irritated the fibres without completely destroying them. At any rate, both the ascending and the descending degeneration was less pronounced on the left side, where the hæmorrhage occurred, than on the right side, where the bundle was cut across without hæmorrhage. This was the only animal in this group that was able to perform circus movements (to the right); it had also conjugate deviation of the head and eyes to the right for six days.

FIG. 2.—Lesion in the region of the corpora quadrigemina posteriores of cat 111.

After the operation, in all these cases of lesion of the middle parts of both posterior longitudinal bundles, there was present on both sides an ascending and descending degeneration in the areas described in the first group, where the lesion was unilateral. A lesion of both longitudinal bundles in the region of the posterior corpora quadrigemina produces forced movements in a vertical plane coinciding with the longitudinal axis of the animal, such as staggering and tumbling, which are not discussed in this paper.

§ 3.—*Lesion of Different Parts of Deiters' Nucleus (Ventral or Triangular Part, and Dorsal or Larger-celled Part) (Table I, Group 3, p. 376).*

We must consider whether the supposition that we have to deal with a vestibulo-mesencephalic tract in the mesial part of the posterior longitudinal bundle is correct; in other words, whether this mesial part is actually identical with the crossed vestibulo-mesencephalic bundle of Fraser, Hösel and van Gehuchten.

For this purpose we have at our disposal two experiments with lesions of different parts of Deiters' nucleus (No. 113, figs. 3*a* and 3*b*, and No. 118), and one with an extensive sagittal lesion lateral to the left posterior longitudinal bundle, and cutting Deiters' complex from the raphe (No. 158, fig. 10). In all three cases we find a degeneration undoubtedly of the same ascending bundle which we described in §§ 1 and 2. The area of the degeneration is exactly the same; it is here found on the side opposite the lesion. The crossing over of the fibres is visible between the level of the distal end of the triangular part of Deiters' nucleus (Fuse) and the decussation of the fourth nerve. This ascending degeneration is more extensive in No. 113 (fig. 3*b*), where the entire triangular part of Deiters' nucleus is cut through, than in No. 118, where it is principally the dorsal large-celled part of the nucleus which is injured. From this we may infer that the crossed vestibulo-mesencephalic bundle originates more especially in the triangular ventral part of the nucleus of Deiters.

Besides this compact bundle on the opposite side, there is a less compact bundle degenerated on the side of the lesion. This ascends in the extreme lateral part of the posterior longitudinal bundle formation (Winkler's fasciculus Deiters ascendens). In No. 158, however, the homolateral ascending degeneration is differently situated. The significance of this ascending degeneration will be considered in Chapter III, §§ 4 and 5.

A comparison of No. 113 with No 118 affords us a special opportunity of determining more exactly the origin of the direct vestibulo-spinal bundle. In No. 118 (lesion of Deiters' nucleus in the narrower sense) this bundle is completely degenerated, although the lesion is limited; in No. 113 (lesion of the triangular part) there is far less degeneration. From this we may conclude that the direct vestibulo-spinal bundle originates more particularly in Deiters' nucleus in the narrower sense, and this agrees with v. Monakow's original

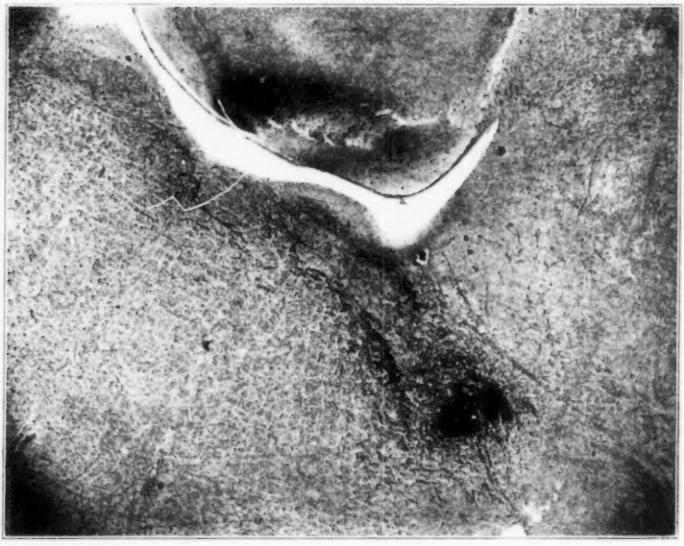

Fig. 3*a*.

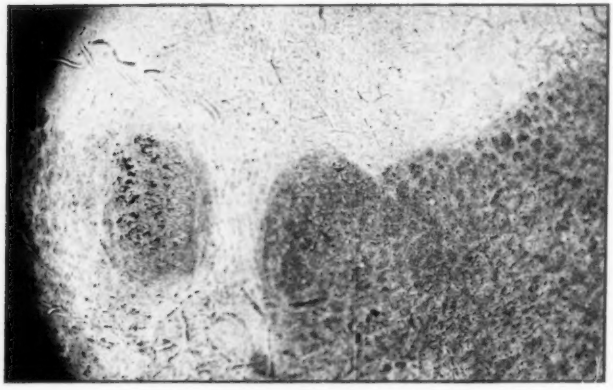

Fig. 3*b*.

FIGS. 3*a*, 3*b*.—Cross sections of cat 113.

Fig. 3*a*.—Stab through Deiters' nucleus.

Fig. 3*b*.—Ascending degenerations in the upper pontine region.

description, and with the findings of Ferrier and Turner, Risien Russell, Thomas, and others.

A descending degeneration in the fibres of the posterior longitudinal bundle also is found on the side of the lesion in any case (particularly after lesion of Deiters' nucleus in the narrower sense). The situation of this homolateral, vestibulo-spinal bundle in the spinal cord is more dorsal and lateral than that of the corresponding crossed bundle. In the region of the cord its fibres intermingle with those of the direct dorsal vestibulo-spinal bundle just described, and which in these cases is also degenerated. This intermingling of the two homolateral descending bundles, their mutual origin from Deiters' nucleus in the narrower sense, and the fact that everywhere in the medulla oblongata degenerated fibres are found, which occupy the intervening space between their two areas, lead us to suppose that these two bundles are identical, both genetically and functionally.

As regards these *homolateral vestibulo-posterior longitudinal bundle-fibres* of Probst, van Gehuchten, and others, I would agree with Thomas and van Gehuchten, that in lesions in the region of Deiters' nucleus one is constantly struck by the great and apparently fundamental differences in the descending degenerations found.[1]

This may be due to the peculiar shape the lesion takes, but it may also be due to the circumstance that Deiters' nucleus, as Kohnstamm has mentioned, is composed of cells of various sizes, which possibly do not all suffer in the like degree from a lesion in this region. Something similar is found in regard to the different bundles of the posterior longitudinal bundle formation, which do not suffer equally when the posterior longitudinal bundle passes through a softened area, for some of the fasciculæ degenerate, and others remain intact [108]. In the same way differences appear to occur in different species in the relative position of the descending bundles, which has led even van Gehuchten to suppose that in the rabbit the homolateral descending vestibular fibres in the posterior longitudinal bundle are missing.

The situation of the homolateral descending Deiters' fibres in the spinal region of the longitudinal bundle is about the same as that of the descending homolateral degeneration, after incision of one posterior

[1] To give a typical example, I would refer to cat No. 7, of Lewandowsky. From the character and situation of the ascending degenerations (both exclusively on the same side as the lesion, cf. § 5 of this Chapter) in the posterior longitudinal bundle formation, there seems to be no doubt that Bechterew's nucleus is affected. Nevertheless one still finds in this case of limited lesion of the *oral* part of the vestibular region the direct vestibulo-spinal bundle considerably degenerated.

longitudinal bundle in the pons region (Chapter I, § 1). In some cases, however, we find the Deiters' fibres more dorsally situated. This fact, coupled with our observations to be referred to presently in regard to the heterolateral descending bundle, makes us question whether it is possible to determine which part of the descending fibres originates in the reticular cells in the region of Deiters' nucleus, and which part in Deiters' nucleus proper. This may be determined possibly by the application of Clarke and Horsley's method of localized lesion. Lewandowsky declared that it was impossible to define Deiters' nucleus sharply from the cells of the reticular formation. The observations of Kohnstamm and Lloyd, however valuable in other respects, did not bring conclusive evidence to bear upon this subject.

Generally speaking, we may say that the course of the crossed ascending vestibulo-mesencephalic bundle, of the direct vestibulo-spinal bundle, and of the homolateral descending bundle in the posterior longitudinal bundle formation, after lesion of Deiters' nucleus, as described by the first authors upon this subject (Held, Ferrier, Turner, Russell, and Thomas), corresponds with the results of the later investigators just mentioned and also with my own, save for the data in regard to the reticulo- or ponto-spinal fibres.

*Heterolateral descending bundles from Deiters' nucleus.* — This matter we shall have to discuss at some length, since opinions differ regarding it.

The cause of these differences of opinion, as far as I can see, is due to the variety of methods adopted in operating, and to the fact that it is not generally recognized that there exist marked anatomical and physiological differences amongst secondary connexions of the different parts of Deiters' nucleus, a circumstance which complicates their analysis very much.

Although we are much indebted to the investigations of Probst, Winkler, and Lewandowsky for our present knowledge of this region, the extensive lesions made by these experimenters cause such widespread degeneration that one is scarcely warranted in drawing definite conclusions in regard to these bundles. Fraser [59] avoids this difficulty by first severing the occipito-atlantal ligament and then incising the most distal parts of Deiters' region with a pointed galvano-cautery. Van Gehuchten experimented with rabbits, and injured, to judge from his figures, the caudal part of the vestibular region, by extracting the facial nerve. Probst's and my own lesions were made by means of a concealed needle piercing the cerebellum; as Horsley and Clarke have

definitely shown that neither from the cortex cerebelli, nor from the intrinsic nuclei do any fibres degenerate directly in the spinal cord, this method seems the most suitable for our purpose.

Wallenberg experimented on pigeons. Although his observations are models of clearness, yet the great disadvantage of experiments upon these birds is the minute extent of the relative parts, so that any advance in the differentiation of the various parts of the vestibular nuclei is not likely from them.

We owe our knowledge to von Monakow and Kohnstamm, and above all to Probst and van Gehuchten that, in addition to a homolateral bundle, there exists also a crossed ponto-spinal or reticulo-spinal bundle, which descends in the area of the posterior longitudinal bundle.

It appears to me that the degeneration of this bundle has interfered to an extraordinary degree with the analysis of numerous experiments, because of the peculiar and capricious shape of its field of origin (Kohnstamm). Thus, for example, I find it degenerated in No. 139 (fig. 1*c*), where there was a sharply defined lesion of the mesial part of the posterior longitudinal bundle (fig. 1*a*), and from this and other experiments I have come to the conclusion that the ganglion-cells for this tract must be present undoubtedly in the immediate vicinity of the posterior longitudinal bundle from below the exit of the sixth nerve (cf. Fraser's monkey, A 2) up to the posterior corpora quadrigemina.

I have shown (No. 93, fig. 5*c*, and No. 95, § 5) that subsequent to a lesion limited to Bechterew's nucleus, there is no crossed descending degeneration of posterior longitudinal bundle fibres, and although in lesions such as those of van Gehuchten's experiments, where the distal part of Deiters' nucleus was involved, there was such degeneration, I do not consider, as I have said, that such experiments can be regarded as conclusive and do not feel justified therefore in assuming with Fraser, Winkler and van Gehuchten, that Deiters' nucleus regularly possesses a crossed descending connexion with the posterior longitudinal bundle. In many cases of lesion of Deiters' nucleus the direct vestibulo-spinal bundle, and also the homolateral Deiters' posterior longitudinal bundle fibres are degenerated, but crossed fibres are lacking, and until some further advance has taken place in our knowledge of the anatomical and physiological relations of this region it is impossible to decide whether any part of Deiters' nucleus, much less what part, gives rise to heterolateral descending fibres.

§ 4.—*Lesion of the Mesial part of the Lateral Horn of the Posterior Longitudinal Bundle (Homolateral Vestibulo-mesencephalic Bundle)* (*Table I, Group* 4, *p.* 376).

In one cat with a lesion low down in the pons region, the larger fibres of the crossed vestibulo-mesencephalic bundle remained intact, but an area lateral to this bundle was degenerated on the side of the lesion (No. 68).

This case appears especially interesting from the fact that hæmorrhage took place exactly in the area of the posterior longitudinal bundle (fig. 4); in this animal there was noted a circus movement, or rather a maximal conjugate deviation of head, neck and eyes to the non-operated side, for thirteen days.

FIG. 4.—Lesion (hæmorrhage) in lateral horn of posterior longitudinal bundle of cat 68.

These degenerated fibres may belong to the area of the crossed vestibulo-mesencephalic bundle; however, Deiters' nucleus of the other side is intact; no descending degenerated fibres in the posterior longitudinal bundle were present except on the side of the lesion and these were situated dorsally and laterally and the direct vestibulo-spinal bundle was not degenerated; moreover, the fibres were of more delicate structure than those of the crossed vestibulo-mesencephalic bundle and were situated more laterally in the posterior longitudinal bundle formation. It seemed, therefore, likely that these degenerated fibres might

have a different origin from that of the crossed vestibulo-mesencephalic bundle.

§ 5.—*Lesion of Bechterew's Nucleus (Table I, Group 5, p. 376).*

This supposition was strengthened as soon as we examined two animals that had sustained a lesion limited to the situation of Bechterew's nucleus (No. 93, figs. 5*a*, 5*b*, 5*c*, 5*d*, and No. 95, figs. 6*a*, 6*b*). In these we found this ascending bundle, and also a bundle of fibres descending in the spinal part of the posterior longitudinal bundle degenerated, but only on the side of the lesion. The origin of this ascending bundle could hardly be other than Bechterew's nucleus. It is then a homolateral vestibulo-mesencephalic bundle (as described by Wallenberg, Winkler and van Gehuchten) which ascends in the direction of the posterior commissure.

The physiological significance of this homolateral ascending bundle which pursues its course lateral to the crossed vestibulo-mesencephalic bundle, appeared closely connected with that of the crossed bundle. This is probable from the fact that animals in which one of these bundles (crossed or uncrossed) was degenerated performed circus movements to the healthy side (*cf.* §§ 1 and 3 of this chapter), or else conjugate deviation of head and eyes (fig. 5*d*) was present.

The homolateral descending fibres of Bechterew's nucleus (less in number in cat 95, where Deiters' nucleus was entirely intact) occupy a more dorsal and lateral position in the spinal part of the posterior longitudinal bundle formation than do the descending homolateral fibres from Deiters' nucleus.

## Chapter II.—A Centrifugal Bundle in the Posterior Longitudinal Bundle-formation which controls Circus Movement to the Side of the Lesion.

Up till now we have become acquainted with two vestibulo-mesencephalic bundles, the mesial one of which is crossed and ascends from the ventral triangular part of Deiters' nucleus, while the lateral one ascends uncrossed from Bechterew's nucleus. The ascending degeneration of either of these tracts and the associated descending degenerations in the spinal part of the posterior longitudinal bundle are apparently always accompanied by circus movements or with conjugate deviation of head and eyes to the non-degenerated side. We

Fig. 5a.

Fig. 5b.

Fig. 5*c*.

Fig. 5*d*.

FIGS. 5*a*, 5*b*, 5*c*, 5*d*.—Taken from cat 93.

Fig. 5*a*.—Lesion in the region of Bechterew's nucleus.

Fig. 5*b*.—Ascending degeneration in the mesial part of the lateral horn of the posterior longitudinal bundle in the upper pontine region.

Fig. 5*c*.—Descending degeneration in the upper dorsal region of spinal cord.

Fig. 5*d*.—Photograph of cat 93, taken thirteen days after operation. Note conjugate deviation of head and eyes towards the left side.

Fig. 6*a*.

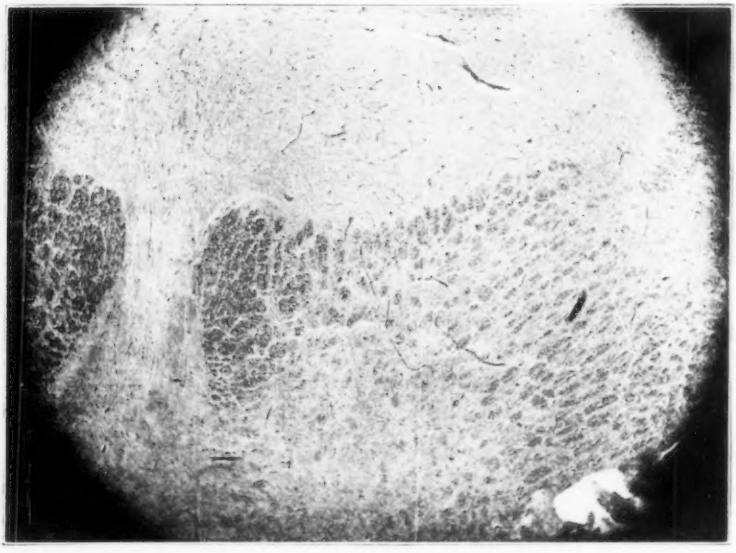

Fig. 6*b*.

FIGS. 6*a*, 6*b*.—Cross sections of cat 95.

Fig. 6*a*.—Lesion in the region of Bechterew's nucleus.

Fig. 6*b*.—Ascending degeneration in the upper pontine region.

have now to determine, therefore, whether our experiments afford any support for the theory, so constantly advanced by recognized authorities, that the posterior longitudinal bundle and its connexions should be looked upon as the pathway of the reflex mechanism for the maintenance of equilibrium. This supposition has been discussed by Edinger, Bleuler, R. Russell, v. Bechterew and Wallenberg, and has been definitely accepted as correct by Spitzer and Kohnstamm. From a clinical point of view, arguments in support of it have been advanced by Prévost, v. Monakow, Spitzka, Gowers, Gee, Tooth, Kaplan, Finklenburg, and others, and these have been accepted on anatomical grounds by Bielschowsky, Bertelse and Rönne, and Lewandowsky. We would consider it our duty, therefore, to examine specially our present material, in order to determine whether it justifies us in dismissing the idea as purely hypothetical, or whether it contributes any definite experimental proof in support of this theory which has been arrived at by such a variety of physiological, pathological and clinical means. It would be a strong argument for the conception of the posterior longitudinal bundle as a pathway for the mechanism of the equilibrium of motion in the horizontal plane, if we were to find that the bundle also contains fibres, the descending degeneration of which is associated almost constantly with circus movements.

With this object in view, we naturally turn our attention to the region where our ascending bundles terminate, and which is obviously closely connected with forced movements, namely, the region of the posterior commissure. We must first determine, therefore, what are the physiological and anatomical consequences of a lesion in this region, and then particularly look for the descending degenerations in the posterior longitudinal bundle, consequent to those lesions, that were associated with circus movements.[1]

For this purpose we have at our disposal seven of my own experiments (Nos. 107, 108, 106, 109, 98, 61, Table II, Group 10, p. 378).

[1] The origin and termination of two descending bundles had already been recognized by myself for some time, and they had been termed fasciculus commissuro-medullaris and fasciculus interstitio-spinalis, not only in my article in the *Nederl. Koninklijke Academie* of October and November, 1912, but also in the manuscript which I sent in December, 1912, to the editor of *Neuraxe*, together with a table and rough outlines of the results of twenty-five experiments; these latter only were published in that journal. My communication concerning circus movements was published in the *Neuraxe* of January, 1914. Since then v. d. Schueren has confirmed the existence of the commissuro-medullary and interstitio-spinal bundle (*Neuraxe*, May, 1913).

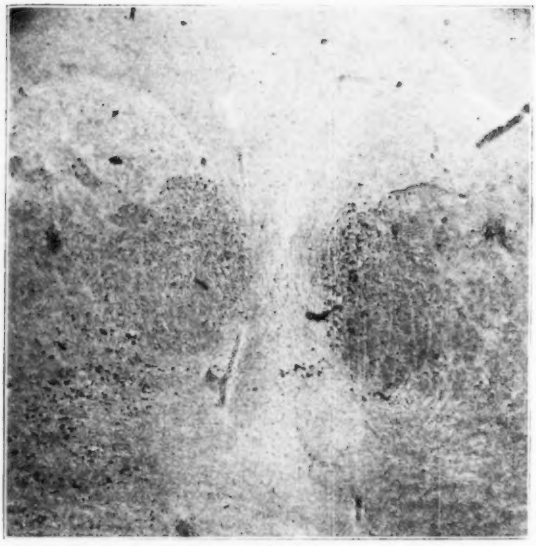

Fig. 7a.

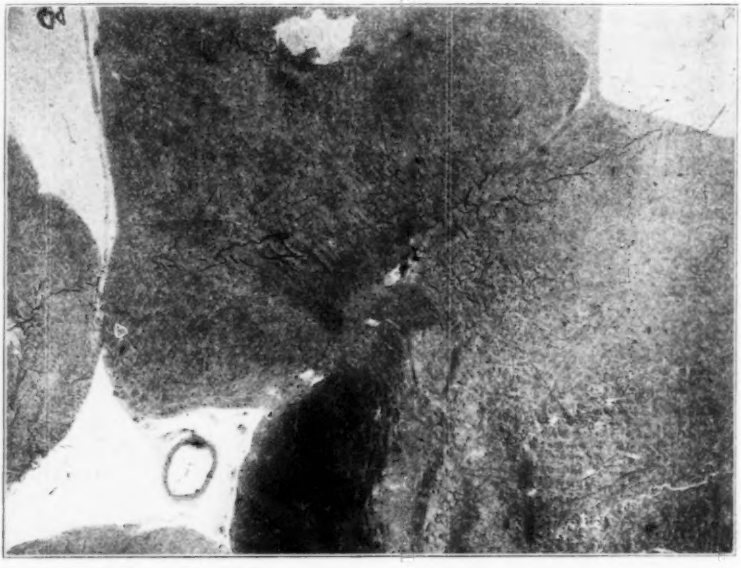

Fig. 7b.

Figs. 7*a*, 7*b*.—Cross sections of cat 108.

Fig. 7*a*.—Descending degenerations in the posterior longitudinal bundles in the region of the trochlear nucleus. Note on the right side the coarse-fibred tractus interstitio-spinalis, on the left the fine-fibred tractus commissuro-medullaris.

Fig. 7*b*.—Descending degenerations in the medulla oblongata. Note on the right side presence of coarse-fibred fibres; no degeneration on the left.

By reference to Table II we notice that, again in accordance with the law of Schiff and Probst ("a hemisection in the caudal parts of the optic thalamus causes circus movements to the side of the operation"), five of these animals executed circus movements to the side of operation for longer or shorter periods. Cat No. 108 was an exception, as it performed rolling movements to the left side or side of operation for a very unusual length of time and circus movement to the left side for one day only. This case exhibited an extraordinary localization of the lesion, which caused degeneration of the commissuro-medullary bundle on the left, and of the interstitio-spinal bundle on the right side (figs. 7*a*, 7*b*).

In this connexion we would recall that in the year 1881 v. Bechterew had already noted circus and rolling movements after lesion of this region; these he afterwards described in detail [11]. Lewandowsky [89] (p. 137), obtained similar results. Both these writers remark, and rightly, that these movements are never characterized by the vehemence which so regularly occurs after lesion of the vestibular region.

A delicately granuled tract was found more or less degenerated in all these five animals, on the side of the lesion, in the mesial part of the posterior longitudinal bundle. In No. 61 it was on both sides of the middle line as the results of the bilateral character of the lesion.

Before proceeding to correlate the anatomical data and the physiological consequences observed, we must exclude any accidental injury of the vestibular nerve, as even limited lesions in its area are so peculiarly liable to bring about forced movements (*cf.* Chapter III, §§ 1, 2, & 3).

In No. 106, for example, we find the nervus vestibularis on the left side slightly speckled with black dots, a condition similar to what was observed in No. 61. If, however, we remember that a lesion of this nerve invariably produces rolling movements to the side of the lesion, we can safely set aside the objection that the circus movements to the right and the left in this group of animals which we are considering, were due to an indirect lesion of the nerve root. It is also unlikely that the slight speckling of the two vestibular nerves (equally) in No. 108, could cause the prolonged tendency to fall to the left side. In No. 109 numerous delicate black granules were found in the two Deiters' nuclei, and as regards this animal we cannot say positively that the circus movement to the right for one whole day was not owing to this unintentional indirect lesion of Deiters' nuclei.

In regard to five animals then, we have notes of the duration and the nature of the forced movements, and also of the different

Left. Right.

Fig. 8a.

Left. Right.

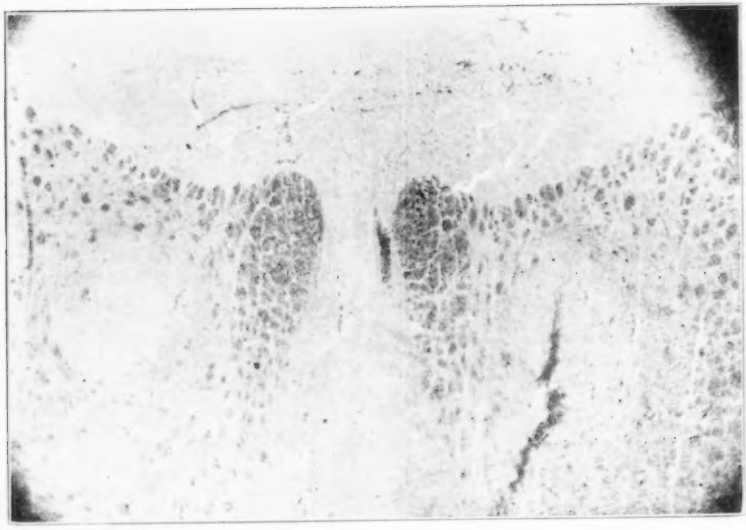

Fig. 8b.

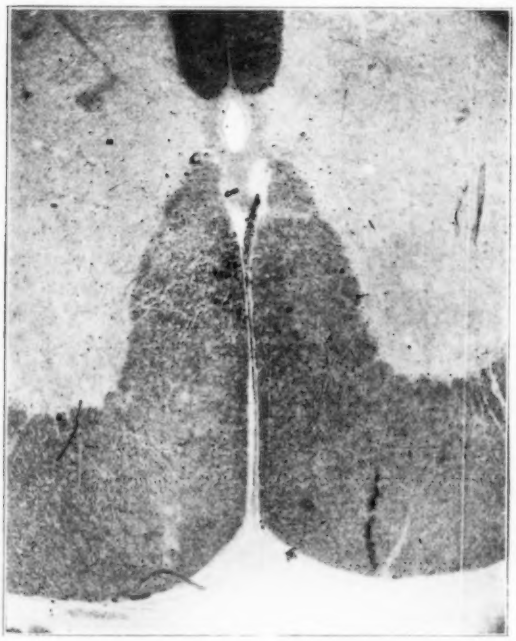


Fig. 8*c*.

FIG. 8*a*, 8*b*, 8*c*.—Cross sections of cat 107.

Fig. 8*a*.—Extent of the lesion at the level of the anterior quadrigeminate body.

Fig. 8*b*.—Level of the nucleus tegmenti profundus. Note the coarse-fibred tractus interstitio-spinalis on the side of the lesion.

Fig. 8*c*.– This same tract in the dorsal region of the spinal cord, on the side of the lesion (by mistake sides reversed).

descending degenerations in the area of the posterior longitudinal bundle, which may possibly be responsible for these movements. The bundle lateral to the posterior longitudinal bundle, as described by Probst, Economo and Karplus, was found degenerated only in Nos. 106 and 108, and was perfectly intact in Nos. 107 and 61, which animals executed distinct circus and rolling movements. From the hypothesis we have mentioned, and which regards the posterior longitudinal bundle as the pathway of a reflex mechanism, we may suppose that there exists a centrifugal component controlling the circus movement. We must investigate, therefore, the condition of the descending tracts within the posterior longitudinal bundle, the lateral bundle having probably nothing to do with these movements.

These descending mesencephalic fibres in the posterior longitudinal bundle, already noted by Held, have been examined after the Marchi method and described by Boyce, Redlich, and Probst in mammals. In them, however, we have to deal with a double bundle, the component parts of which begin and end differently. Their different course was first described in the year 1912 [108], and the bundles were termed the commissuro-medullary and interstitio-spinal bundle. Cajal, Wallenberg, and van Gehuchten discovered the descending mesencephalic fibres of this region in birds and fishes. De Lange studied them in different species of animals, and considered them homologous with the uncrossed tecto-bulbar bundle of the fish. In a rabbit he followed them right into the sacral region. As regards man, centrifugal fibres in the posterior longitudinal bundle have been described by Gee, Tooth and Roussy as being situated in its mesial segment, and, according to Roussy, also in its dorsal part.

Where we can follow this part of the posterior longitudinal bundle in its downward course as in Nos. 107 and 108, we can readily determine that we have before us here two separate anatomical entities; in No. 107 we can follow the interstitio-spinal bundle as a separate strand of coarse fibres well into the lumbar region of the spinal cord (fig. 8*c*). It is situated in the anterior column and runs close to the anterior fissure, about two-thirds of the way from the ventral to the dorsal end of the fissure. On the other hand, in No. 108 we see that the delicately fibred tract on the left side (fig. 7*a*), most mesially situated in the posterior longitudinal bundle, disappears caudally in the abducens nucleus in the oblongata (fig. 7*b*), and only a few solitary fibres from it can be followed into the cervical spinal cord, or lower.

When we now consider (Table II) that in unilateral lesions of the region of the posterior commissure, which are followed by circus movements to the side of the lesion, with conjugate deviation of the head and eyes, we constantly find degenerated fibres in the innermost part of the posterior longitudinal bundle, descending towards the medulla, it thus seems likely that we have here the centrifugal limb of the reflex arc which controls circus movements to the side of the mesencephalic lesion.

We must conclude therefore that in the posterior longitudinal bundle there are found not only two tracts on each side of ascending fibres, the degeneration of which occurs simultaneously with circus movements to the healthy side, but also on each side a centrifugal "final common path" [Sherrington 147], the descending degeneration

of which is associated with circus movements to the side of the lesion. In agreement with this theory of Sherrington's is the circumstance that the ascending fibres of this reflex arc are much more abundant than the descending. The condition resembles that of the single giant Mauthner-fibre of fishes, which, according to Kohnstamm, controls the motion of the tail fin.

None of my experiments is in direct opposition to this supposition; one of Economo and Karplus's experiments also (referred to in Table II) may be regarded as supporting it, and Roussy's [135] results and Kohnstamm's may be interpreted also as in agreement with it.

It is true that I find in some of my thalamic lesions in certain animals the same phenomena as were present in cat No. 1 of Roussy's series. This animal, although the nucleus of the posterior commissure and the commissuro-medullary bundle were intact, performed circus movements towards the operated side for some time. But in Chapter VI this class of experiments will be dealt with especially, i.e., lesions of a tract of fibres that connects the cerebral hemisphere (striate body) with the region of the posterior commissure. To declare, as Roussy does, the degree of circus movement to be in proportion to the injury of the pedunculi, would be neither in accordance with my own results, nor with those of other authors, Roussy's included.

Direct electric stimulation of this region may contribute towards the ultimate solution of this anatomo-physiological problem. This question also will be taken up further in Chapter VI.

## Chapter III.—The Primary and Secondary Vestibular Connexions, and forced Movements in the Plane Vertical to the Longitudinal Axis of the Animal (Rolling Movements).

### § 1.—*Lesion of the Vestibular Root (Table I, Group 6, p. 376).*

In Group 6 of Table I we have included those cases in which the vestibular root itself was injured by the instrument, or was found degenerated to such an extent that some indirect injury to it must have taken place by stretching, or haemorrhage, or in some such way.

The forced movements after direct lesion of the vestibular root, that is to say in the cases with definitely confirmed total degeneration in the nerve-root, are of far longer duration than those after indirect lesions or

| Experiment | Lesion | Duration of life | Circus movement |
|---|---|---|---|
| | *Group I.—Section of the median part of the bundle on one side.* (Compare | | |
| 139 | In middle pontine region, on right side .. .. | 15 days | To the left .. |
| 119 | Region of posterior corpus quadrigeminum, on left side | 7 ,, | To the right .. |
| 91 | Lower pontine region, on left side .. .. .. | 16 ,, | ,, ,, .. |
| | *Group II.—Section of median part of bundle on both sides.* | | |
| 114 | Oral to 4th nucleus .. .. .. .. .. | 21 days | — |
| 97 | ,, ,, .. .. .. .. .. | 6 ,, | — |
| 92 | Both bundles and left lateral horn, in lower pontine region | 14 ,, | Head deviated to right side |
| 90 | Both bundles and right lateral horn, in lower pontine region | 21 ,, | To right side, with conjugate deviation of head and eyes |
| | *Group III.—Lesions of different* | | |
| 113 | Nucleus Deiters (triangular part), on right side .. | 20 days | To the right .. |
| 118 | Nucleus Deiters proper on right side .. .. .. | 28 ,, | ,, ,, (?) .. |
| 158 | Sagittal lesion, cutting off vestibular region from raphe, on left side | 15 ,, | To the left .. |
| | *Group IV.—Lesion of the homolateral* | | |
| 68 | Softening of lateral part of pons: haemorrhage in lateral horn, on right side | 14 days | Maximal conjugate deviation to left |
| | *Group V.—Lesions of* | | |
| 93 | Bechterew's nucleus and dorsal part of crus cerebelli ant., on right side | 28 days | Tendency to walk to left |
| 95 | Bechterew's nucleus and nucleus brachii pontis sup., on right side | 24 ,, | To the left .. |
| | *Group VI.—Lesion* | | |
| 23.5.00 | Acustico-vestibular region, on right side .. .. | 28 days | Head turned to right |
| Rabbit V | Extirpation of so-called flocculus, on right side .. | 11 ,, | — |
| 42 | Acustico-vestibular exit, on right side .. .. | 33 ,, | — |
| 67 | Destruction of nucleus vestibularis and ganglion ventrale, on right side | 20 ,, | — |
| | *Group VII.—Lesion of Ramus* | | |
| VIII | Cyst in caudal part of ram. desc. viii, on right side | 34 days | — |
| 18 | Flocculus cerebelli, corpus restiforme, and ram. desc., on right side | 11 ,, | To the right .. |
| 35 | Corpus restiforme, nucleus desc. v and viii, softened, on left side | 34 ,, | — |
| 146 | Sagittal lesion through caudal part of corpus trapezoides, on right side | 13 ,, | Tendency to walk to left |
| 158 | Compare Group III. | | |
| | *Group VIII.—Lesion of Deiters' nucleus.* | | |
| | *Group IX.—Lesion of lateral horn of posterior longitudinal bundle.* (Compare Group | | |
| 62 | Incision in crus cerebelli ant., and lateral horn, on right side | 14 days | — |
| 150 | Lesion of lateral part of lateral horn, on right side | 15 ,, | — |
| 221 | Two punctures through lateral horn, on left side .. | 14 ,, | Head bent to left(?) |
| | *Group X.—Lesion of median part of lateral horn of posterior longitudinal* | | |
| | No. 158, and Cat 5 | | |

| Duration | Rolling movement | Duration of movement | Area of P.L.B. to 4th nucleus |
|---|---|---|---|
| Probst's Case IX [123, p. 72] and Economo's Case V [78, p. 411].) | | | |
| 10 days | .. .. .. .. .. .. .. | — | |
| 2 ,, | .. .. .. .. .. .. .. | — | |
| 8 ,, | Falls on right; lies down on right side .. | 14 days | |
| (Compare Fraser's Monkey No. 2 [59, p. 383].) | | | |
| — | Staggers .. .. .. .. .. .. | — | |
| — | "Tumbling"; falls to left and right .. .. | 5 days | |
| 4 days | Falls to left; eyes rotated to left .. .. | 4 days; 12 days | |
| 9 ,, | Head rotated to right .. .. .. .. | 2 days | |
| *parts of Deiters' nucleus.* | | | |
| 8 days | Head rotated to right .. .. .. .. | 8 days | |
| 1 day | Falls to right .. .. .. .. .. | 7 ,, | |
| 9 days | .. .. .. .. .. .. .. | 11 ,, | |
| *vestibulo-mesencephalic bundle.* | | | |
| 10 days | Lies on left side .. .. .. .. .. | Few days | |
| *Bechterew's nucleus.* | | | |
| 6 days | Rolls to right; falls to right .. .. .. | 8 days; 22 days | |
| 5 ,, | .. .. .. .. .. .. .. | — | |
| *of vestibular root.* | | | |
| 25 days | Rolls and falls to right; lies on right side | 28 days | |
| — | Head rotated and bent to left .. .. | 11 ,, | |
| — | Vehement rolling to right; rotation of eyes | 33 ,, | |
| — | ,, .. .. ,, ,, | 20 ,, | |
| *descendens nuclei vestibularis.* | | | |
| — | Rolls to left; head and eyes rotated to left | 2 days; 4 days | |
| 3 days | Rolls to left .. .. .. .. .. | 3 days | |
| — | Tendency to roll to right .. .. .. | 12 ,, | |
| Some days | Slight tendency to roll to left .. .. | Some days | |
| (Compare Group III, Nos. 113 and 118.) | | | |
| II, Nos. 90 and 92; Group V, No. 93, and Kohnstamm's Rabbit IV [81].) | | | |
| — | Rolls to right .. .. .. .. .. | 6 days | |
| — | .. .. .. .. .. .. .. | 5 ,, | |
| 1 day | Lies down exclusively on left side .. .. | 3 ,, | |
| *bundle.* (Compare Group I, No. 91; Group IV, No. 68; Group VII, of Karplus [78].) | | | |

TABLE II.—CENTRIFUGAL TRACTS IN

| Experiment | Lesion | Duration of life | Fasc. commissuro-medullaris | Circus movement |
|---|---|---|---|---|
| 107 | Lesion of lateral part of posterior commissure (middle division), on right side | 11 days | Degenerated on right side | To the right |
| 108 | Region antero-lateral to red nucleus, on right side | 18 ,, | Degenerated on left side | To the left |
| 106 | Extreme antero-lateral part of posterior commissure, on right side | 21 ,, | Few fibres, right > left | — |
| 109 | Extreme oral part of posterior commissure, on right side | 17 ,, | ,, ,, | Tendency to walk to right |
| 98 | Lesion of latero-posterior part of posterior commissure, on right side | 19 ,, | Degenerated on right side | To the right |
| 61 | Region of posterior commissure, on right and left sides | 26 ,, | Left > right.. | Tendency to walk to left |

Compare also Probst's Case [123, p. 527], Besta's Cat [17, p. 417].

than the forced movements described in the first two chapters of this paper. Also the character of the rolling associated as a rule with the Hertwig-Magendie squint (the eyeball of the side of the lesion being deviated downward, that of the other side being directed upward) is far more vehement in the case of a direct root lesion. In cats it is only after direct injury of the vestibular nerve that rolling movements continue for weeks; after secondary or indirect lesions of the vestibular nerve, and *a fortiori* after lesion of the ascending systems only, minor phases only of forced movements were noticed, such as a tendency to lie on one side, to fall to one side, or a rotation of the head to one side, when the chin was moved away from the direction of the rolling.

As soon as the anæsthesia passes off in lesions of the vestibular root, there occurs usually a rotation of the eyeballs on their antero-posterior axis towards the side of the lesion, a rotation which is easily demonstrated in cats because of the slit-like shape of the pupil, and in rabbits can be made apparent by the performance of a preliminary iridectomy [107]. The upper half of both eyeballs is seen to be rotated towards the side of the lesion, the lower half from the side of the lesion. Further nystagmoid movements of the eyeballs can be observed, slow in character in the direction of the rotation, but rapid in character in the opposite direction. This rotatory nystagmus usually lasts for a few days only, and is increased by turning the head in the direction *opposite* to that of the rotation.

After compensation of the rolling movements has taken place, they may be renewed by blindfolding the animal. For a long time

POSTERIOR LONGITUDINAL BUNDLE.

| Duration | Fasc. interstitio-spinalis | Rolling movements | Duration of movements | Area of P.L.B. |
|---|---|---|---|---|
| 8 days | Degenerated on right side | Head rotated to left side | 8 days | |
| 1 day | Degenerated on right side | Tendency to fall on left side | 9 ,, | |
| — | — | .. .. .. .. | — | |
| Few hours | Few fibres (?) .. | .. .. .. .. | — | |
| 1 day | Few fibres on left > right | Slow rotatory jerks to right side | Few hours | |
| 3 days | — | Slight tendency to roll to right side | 3 days | |

and Karplus's Cat 3 and Macacus 3 [78, pp. 298 and 342].

the animal can also be pressed down more easily to the side to which he tended to roll than to the other side. By Marey's falling experiment (the normal cat on being taken up by its legs, and dropped, invariably lands upon its paws) the rolling can be brought about again, and in epileptic fits it may also recur. It is remarkable, however, that in ether narcosis a rotation in the opposite direction [137, cf. also 133] is observed.

In studying this group of animals (Group 6) we notice that, with the exception of rabbit V, the rolling movements invariably occurred in such a manner that the locomotion was always to the side of the injured vestibular nerve. This accords with the earlier experiments of Flourens, Schiff and Cyon, and with those of Ewald, Breuer, Winkler, Camis, Bartels, and others of later date, dealing with lesions of the semicircular canals and section of the nervus acustico-vestibularis.

It is outside the province of this paper to discuss the hydrokinetic theory of these organs, simultaneously brought forward by Crum Brown, Breuer and Mach, or to recall the extensive literature concerned with stimulation experiments performed upon the semicircular canals and the acoustic maculæ. I will merely remark that a lesion of one canal tends to produce deviation or movement in the plane of that canal as well as corresponding alterations in the compensatory changes in position of the eyeballs that take place during movements of the body [31, 70, 84, 87] (pathological observations of Stein, Stenger, Bourgois, Bezold, van Uffenorde). It is well known

that not only in vertebrates, but also in invertebrates, for example in octopods (v. Uexkull, Muskens [110] Prentiss), removal of the whole otolitic organ invariably causes rolling movements to the side of the lesion, together with corresponding disturbance of independently moving parts of the body (eyeballs, fins, tail, &c. [18, 93]).

As regards the more recent researches concerning the vestibular nerve itself, I would quote those of Biehl [21], relating to direct electrical stimulation of this nerve in horses and sheep. During the stimulation, for instance, of the right nerve, a deviation was observed of both eyes to the right side, with small rapid nystagmus in the same direction; at the same time there was a squint present, the left eye being below, the right above, a deviation which is found in animals that roll to the left side. Immediately after severance of the vestibular nerve, on the other hand, the deviation of the eyeballs and the squinting were in exactly the opposite direction; thus, after section of the right root, the horizontal deviation of the eyes was to the left, the left eye was turned upwards, and the right downwards. To conclude, as Biehl does, from these observations (which are partially at variance with those of some experienced physiologists) that the stimulation experiment indicates the character of the normal working of the vestibular nerve appears hardly justifiable. We should rather assume that the vestibular root comprises so many different physiological entities, all in connexion with the preservation of static and dynamic equilibrium, that it will depend upon the details of the experiment as to what results will ensue from stimulation or injury of the root. Thus from my own experiments it would appear that a lesion of the proximal parts of the vestibular nuclei causes forced movements, the direction of which may be the reverse of that of movements caused by lesion of the caudal parts of the nuclei. It would, therefore, hardly be surprising if direct stimulation of the proximal and caudal fibres of the root produced oppositely directed conjugate deviations. Stimulation and section of the whole of the vestibular root gives evidence, I consider, of the function of the preponderant semicircular canal in that particular animal.

As regards the anatomical results in this group of animals we are considering, I must make particular mention of rabbit V, where the pars petrosa cerebelli, according to Bolk [26], or the so-called flocculus was extirpated, and a part of the vestibular nerve was injured, an associated lesion which occurs very rarely with this operation. Amongst a large number of experiments I consider this case the only one which can be utilized for the study of the intracerebral degeneration that occurs after a lesion of the vestibular root alone, since all other experiments in rabbits and cats showed, on careful microscopic examination, complications caused by associated lesions in adjoining regions. In this animal we could follow the degenerated vestibular nerve-sheaths

into three cell groups, to the descending ramus of the vestibular nucleus, to Deiters' nucleus (both to its ventral distal division—nucleus triangularis—and to its dorsal large-celled division—Deiters' nucleus in the narrower sense), and to the region of Bechterew's nucleus and the nucleus tecti [112]. Meynert, Sala and Thomas also traced vestibular fibres directly into the roof nuclei.

In none of my numerous experiments with lesions of the vestibular nerve could I succeed in following the course of the root-fibres towards the area of the posterior longitudinal bundle and its lateral horns, or towards the pons or mid-brain, or descending directly into the spinal cord. In vain did I endeavour to convince myself, by means of the osmic acid method, of the existence of direct vestibular fibres which cross the raphe (Cajal and Wallenberg in birds, Deganello [46] in frogs, Lewandowsky in mammals). I should almost doubt that such fibres exist, although the silver method of Cajal strongly suggests them; what may happen, with the osmic acid method, I think, is that in extensive injury of the elements of the vestibular nerve, a few fibres originating from Deiters' nucleus degenerate upwards, and thus simulate direct root-fibres. Further, I cannot agree with Lewy [91] that the structures in the posterior longitudinal bundle are more likely than those in other regions to contain fibres coloured by osmic acid. On the contrary, by carefully avoiding all compression of the brain, I have obtained ample proof that even extensive lesions of the cerebellum (including the nucleus dentatus) never cause the slightest degeneration in the posterior longitudinal bundle: in these cases I never observed the slightest sign of forced movements in the two planes (circus movement in the horizontal plane, and rolling movement in the vertical plane, vertical to the long axis of the animal) which are discussed in this paper.

As regards the striking difference in the physiological effects produced by the lesion in rabbit V, and those produced by all the other lesions of the vestibular root, I must observe again that the rolling movements in this case were never of a vehement character, and, as already stated, were directed to the side opposite to the lesion. Seeing that this sort of rolling movement never resulted in numerous other rabbits in which the flocculus alone was removed, together with the part of the nucleus dentatus enclosed in it [114], it must probably depend in this case upon the unusual lesion of the vestibular root that was present. In this case (rabbit V) it was especially the caudal part of the vestibular root and the ramus descendens that were degenerated,

and the limited extent of the lesion is proved by the absence of degeneration in the tuberculum acusticum and the corpus trapezoides.

### § 2.—*Lesion of the Descending Ramus of the Vestibular Nucleus (Table I, Group 7, p. 376).*

The next group to be considered contains the animals with lesion of the descending ramus of the vestibular nucleus; either a total destruction of the cell area as in cat No. 8 (fig. 9) or a partial lesion as in Nos. 18 and 35. The chief point in connexion with this lesion is that

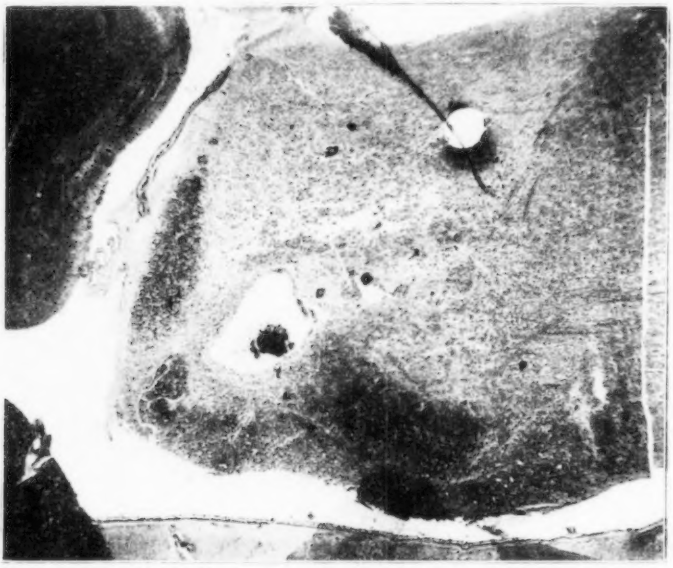

FIG. 9.—Lesion of the medulla oblongata of cat 8, softening with cystic degeneration, including the ramus descendens nuclei vestibularis.

in these cases rolling movements to the healthy side, or at any rate an inclination thereto, were observed during the life of the animal. The intensity and the duration of these rolling movements and of the corresponding deviation and rotation of the eyeballs around their axes that accompanied them [107, 113] appear to be in direct proportion to the intensity of the lesion in this part of the vestibular complex, or to the completeness with which, as in some other experiments, this part

of the complex is cut off from the raphe, and from the more proximally situated parts of the cerebrum.

In cat No. 8 we have to deal with a complete cystic degeneration of the entire region (fig. 9). In cats Nos. 18 and 35, the lesion is partial only and caused apparently by indirect temporary pressure; in the latter of these two animals rolling movement never actually ensued. In cat No. 146 it was the distal part of the ramus descendens only that was cut off from the raphe and the proximal parts of the brain; in cat No. 158 the sagittal lesion was immediately lateral to the left posterior longitudinal bundle and severed the entire vestibular region from the raphe (figs. 10*a* and 10*b*). This last animal fell for several days towards the side opposite the lesion.

I must admit that my material is inadequate to allow the conclusion to be drawn absolutely that this part of the vestibular system specially controls this function of rolling movements towards the non-severed side, or rather this negative function, because, according to Munk [106] rolling movements are to be considered as the result only of an inability to maintain the normal posture. However, I consider this conclusion is in accordance with the facts so far obtained by a physiological analysis of the Deiters' complex, and it is such a relatively rare occurrence that, after a lesion of the descending ramus, an animal remains alive long enough to admit of observations being made, that I consider these preliminary results worth noticing. I have to confess that all the lesions in this group involved accidentally the ramus descendens. Only once did I succeed in my attempts to produce a lesion of the descending branch and in this way to observe rolling movements towards the healthy side.

As regards the secondary degenerations which are due to a lesion of the ramus descendens, it is only in No. 158 that I have been able to obtain positive (?) data. In this animal an ascending degeneration is present in the mesial part of the lateral horn of the posterior longitudinal bundle (fig. 10*b*), but the situation and the extent of the sagittal lesion in this case are not such as to justify us in concluding that this ascending bundle actually originates in the ramus descendens of the vestibular nucleus: probably it is the one which was affected in the case discussed in § 5 of this chapter. This much is certain, however, that in cat No. 8, with a complete destruction, and in cat No. 18, with a slight lesion of the ramus descendens, there is strangely enough only the merest trace of ascending degeneration in the heterolateral posterior longitudinal bundle, and at the same time only exceedingly

Fig. 10*a*.

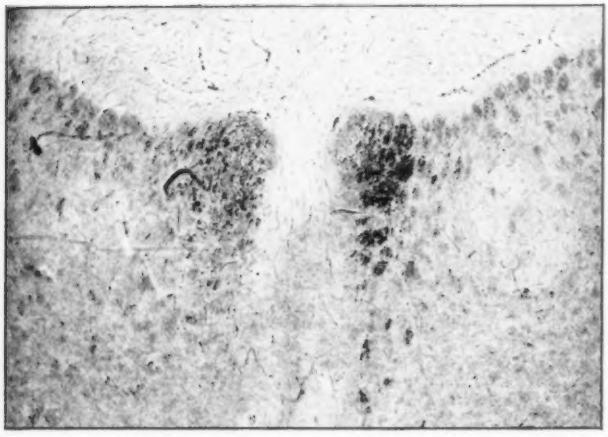

Fig. 10*b*.

FIGS. 10*a*, 10*b*.—Taken from cat 158.

FIG. 10*a*.—Sagittal lesion on the left side of the posterior longitudinal bundle, cutting off the vestibular region from the raphe.

FIG. 10*b*.—Ascending degeneration in the region of the nucleus tegmenti profundus. Note also degeneration of the tractus vestibulo-mesencephalicus cruciatus.

slight descending degeneration either on the side of the lesion or on the opposite side. As to No. 158 the degenerated fibres may be merely crossed ones.

In the literature I find certain facts which are in support of my views. This is the case in the discussion by Longet [94] on the rolling movements which occur after a lesion behind the fifth nerve. Luciani and Sergi [96] confess that they cannot explain why, after lesion of the lower posterior part of the cerebellum, rolling movements should appear which take an opposite direction to those seen after ablation of a hemisphere. Russell [138] observed the same movements after lesions of the restiform body.

As it is impossible for a lesion to be confined absolutely to the ramus descendens, the restiform body being usually involved, it might be suggested that the ascending olivo-cerebellar fibres took part in this phenomenon. If, however, it be considered certain that all the olivo-cerebellar fibres terminate in the cerebellar cortex, the fact that no lesion of the cerebellar cortex alone is associated with the demonstration of this phenomenon renders the supposition improbable.

### § 3.—*Lesion of Deiters' Nucleus* (*Table I, Group* 8, p. 376).

In two animals (Nos. 113 and 118) the lesion was limited to Deiters' nucleus on the right side (Group 8 of Table I). In both these animals, circus movement to the side of operation was observed. In Chapter I, §§ 1 and 3, I have discussed the crossed ascending degeneration of fibres, passing from this nucleus into the posterior longitudinal bundle, and in these two animals there was also a falling movement to the side of the lesion as well as a circus movement. In both animals ascending degeneration was found in the most lateral part of the lateral horn of the posterior longitudinal bundle, and could be followed in an upward direction as far as the region of the tegmentum. A few fibres, however, could be followed into the posterior commissure at its extreme caudal level (lateral fibres seen in fig. 3*b*, on right side).

In § 4 of this chapter, it is shown that a direct lesion of the lateral part of the posterior longitudinal bundle is followed by an ascending degeneration of the fasciculus vestibulo-tegmentalis lateralis, which is in all cases accompanied by rolling movements towards the side of the lesion.

After a careful examination of the cases and their anatomical lesions, one feels bound to admit that different parts of Deiters' nucleus control

the circus movements to the operated side, and the rolling movements towards the side of the lesion. This is illustrated in cases Nos. 113 and 118. In the first case the circus movements lasted a whole week, while in the second they were present for one day only; in the first case the entire caudal triangular part of Deiters' nucleus was injured, and the ascending crossed vestibulo-mesencephalic bundle was far more extensively degenerated than in the second case. From the physiological analysis one may further deduce that the magno-cellular part of Deiters' nucleus, or what is termed Deiters' nucleus in the narrow sense, which controls the rolling to the side of the lesion, sends out more descending fibres towards the spinal cord on the side of the lesion, than the ventral part which controls the circus movements to the side of the lesion.

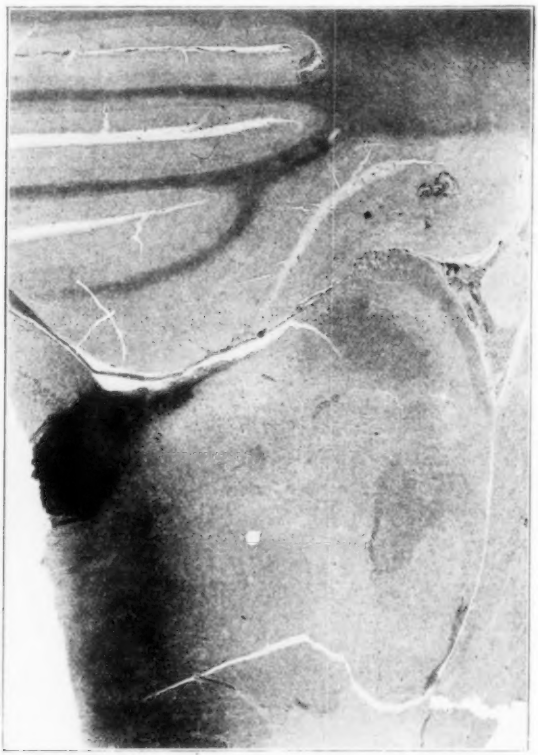

Fig. 11*a*.

Fig. 11*b*.

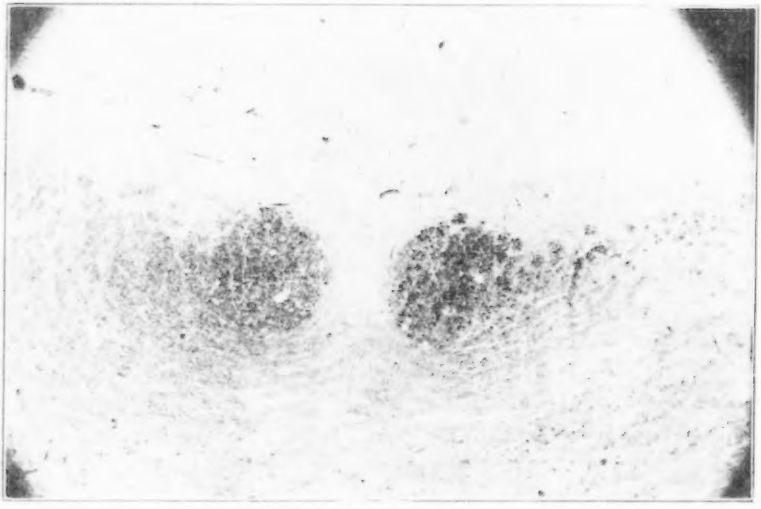

Fig. 11*c*.

FIGS. 11*a*, 11*b*, 11*c*.—Cross-sections of cat 90.

Figs. 11*a* and 11*b*.—Lesion of the posterior longitudinal bundles in the pontine region. Note destruction of the lateral horn on the right side.

Fig. 11*c*.—Ascending degeneration of the lateral horn on right side.

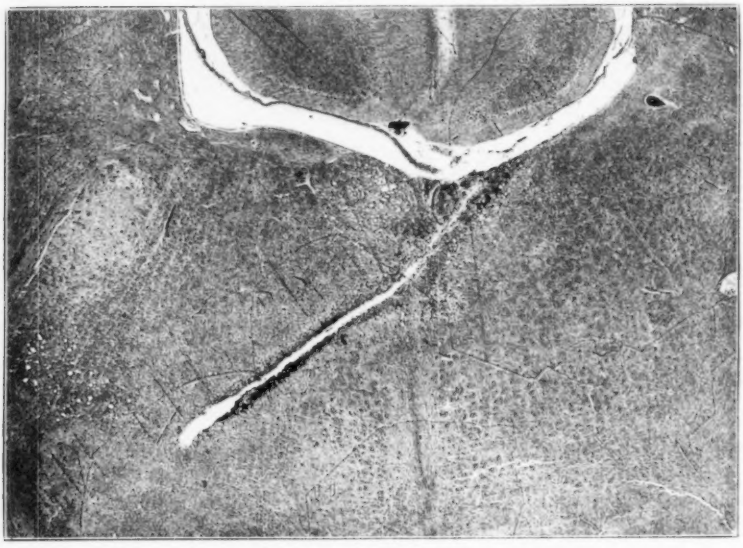

FIG. 12*a*.

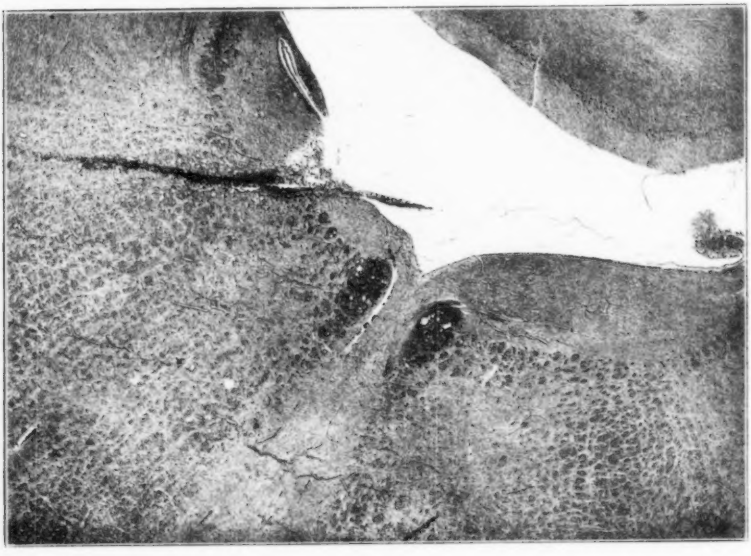

FIG. 12*b*.

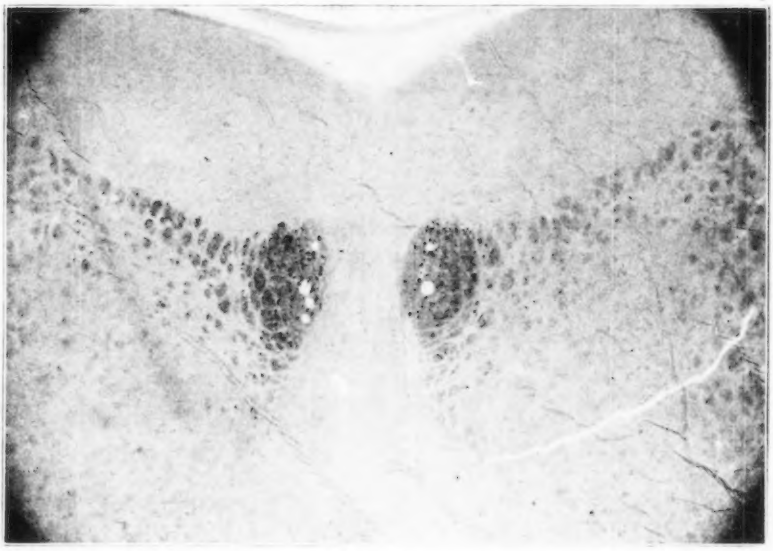

Fig. 12c.

Figs. 12*a*, 12*b*, 12*c*.—Cross-sections of Cat 92.

Figs. 12*a* and 12*b*.—Lesion of the posterior longitudinal bundles in the pontine region. Note destruction of the lateral horn on the left side.

Fig. 12*c*.—Ascending degeneration of lateral horn on left side.

As has already been pointed out in Chapter I, § 3, it has not yet been possible to determine which part of the homolateral, and particularly of the heterolateral descending posterior longitudinal bundle fibres originate in the reticular cells (fasciculus reticulo-spinalis), and which from Deiters' nucleus.

§ 4.—*Lesion of the Lateral Horn of the Posterior Longitudinal Bundle (P.L.B.) or Fasciculus Deiters' Ascendens (F.D.A. of Lewandowsky and Winkler)* (*Table I, Group* 9, p. 376).

The following groups of experiments (Groups 9 and 10) concern the direct lesions of the lateral part of the posterior longitudinal bundle), which is acknowledged by Winkler [169], Lewandowsky [89], and van Gehuchten [63], to be an anatomical entity, and named by them the fasciculus Deiters' ascendens (F.D.A.), or faisceau triangulaire.

Special attention should be paid to experiments Nos. 90 and 92 (cf. the diagrams of the table, Group 2, and the figures 11*c* and 12*c*),

because in those animals both the posterior longitudinal bundles were cut between the sixth and fourth nuclei. In No. 90 the *right* fasciculus Deiters' ascendens was also cut (figs. 11*a*, 11*b*), while in No. 92 the *left* fasciculus Deiters' ascendens was cut (figs. 12*a* and 12*c*).[1]

We here observe a remarkable parallelism between the physiological and anatomical data given in the table. In Case 90, where the right fasciculus Deiters' ascendens was severed, it showed degeneration upwards to the right, while the animal displayed a rolling movement to the right side. In Case 92 the left fasciculus Deiters' ascendens showed degeneration upwards to the left, while the animal also displayed a rolling movement to the left side.

In not a single case was there any trace of a lesion in either the vestibular root, Deiters' nucleus, or the ramus descendens of the eighth nucleus, which might be the cause of this phenomenon.

In Case 114 both the posterior longitudinal bundles were severed orally to the fourth nucleus, while the right fasciculus Deiters' ascendens was also cut. In this case it was only in epileptic fits induced by camphor monobromate that falling to the right side was observed.

In the next five experiments the extreme lateral part of the fasciculus Deiters' ascendens was either injured directly, or it was found degenerated in consequence of a lesion of Deiters' nucleus associated with extirpation of a cerebellar hemisphere.

In some cases, such as No. 150 (cf. also Quensel's case No. 1 [128]), only the extreme lateral fibres of the fasciculus Deiters' ascendens were affected on one side, yet the animal showed a decided tendency to fall to the same side. In such cases the ascending degeneration can only be followed for a short way, which evidently shows that these lateral fibres lose their sheaths immediately they enter the region of the posterior commissure.

It is not necessary to go further into detail concerning these experiments, seeing that the diagrams of the table (Group 9) furnish all the necessary data.

From a consideration of the data it seems probable that there is a vestibular ascending bundle (or one of several such bundles) in the lateral part of the fasciculus Deiters' ascendens, which controls the

[1] As regards the circus movements to the right shown by Case 90, it should be remembered that in this animal hæmorrhage ensued into the posterior longitudinal bundle, which presumably caused an unequal lesion of the mesial parts of the posterior longitudinal bundles, causing circus movement.

rolling movements to that side. This bundle may be termed the fasciculus vestibulo-tegmentalis lateralis.

From the results obtained after lesion of the principal division of Deiters' nucleus (Chapter III, § 3), it may be deduced that the medium or small cells of the dorsal division of Deiters' nucleus (that is Deiters' nucleus in the narrow sense) constitute the origin of this bundle. This conclusion is come to in consequence of the total degeneration of the giant cells seen after hemisection of the cervical cord (v. Monakow [104]).

In numerous other lesions made in the pontine region I have never observed any rolling movement when the vestibular nuclei and their ascending systems remained intact. I can further confirm for one experiment the observation of Spitzer and Karplus [150], that a longitudinal incision in the middle cerebellar peduncle is not associated with circus movements.

### § 5.—*Lesion of the Mesial Part of the Fasciculus Deiters' Ascendens* (*F.D.A.*). (*Table I, Group* 10, p. 376).

Among the numerous experiments in which lesions were made in the region oral to the Deiters' nucleus, there are certain cases which are in apparent conflict with the results discussed in the foregoing paragraph as regards the physiological phenomena, and also, I believe, as regards the anatomical data.

In none of these cases did the rolling movements actually appear. At most there was a tendency for the animal to roll or fall on to the non-operated side. In Case 91 there was found only a slight degeneration of the left vestibular root and of the right Deiters' nucleus which might possibly account for this phenomenon.[1]

In the other cases I can assign no cause for this tendency to fall towards the normal side.

In these three cases under consideration there is an ascending degeneration predominating in the mesial part of the fasciculus Deiters' ascendens which appears to me to afford good ground for supposing that

[1] Although I have considered it necessary for the physiological analysis of the posterior longitudinal bundle to exclude all the cases in which collateral injury of the vestibular roots and Deiters' nucleus occurred, it yet appears highly improbable in Case 91 that the slight lesion of these parts was the cause of the protracted inclination to fall to the non-operated side. If we accept this, the case would bear out what is maintained in this paragraph. In Case 68 the objection is justified that the same injury which caused degeneration of the descending fifth root and of the restiform body on the right side, may have involved the descending eighth root on the same side.

there is an ascending vestibular connexion with this part of the fasciculus Deiters' ascendens, which controls the rolling movement to the healthy side (fig. 13).

In these cases there is a moderate descending degeneration in the spinal posterior longitudinal bundle of the same side, down to the dorsal region.

There are, however, too few cases to allow of any positive conclusions being formed as to the existence of such a bundle.

Should further investigation, however, confirm this supposition, the bundle might appropriately be named the fasciculus vestibulo-tegmentalis medialis. (Cf. the ascending degeneration in the posterior longitudinal bundle on the left side in Case 91, fig. 13, and Case 158, fig. 10*b*, respectively.)

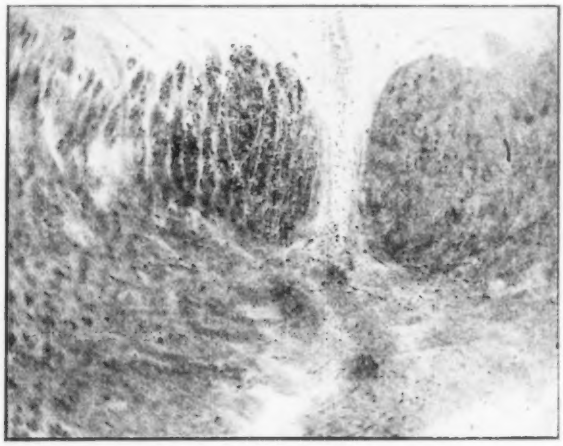

FIG. 13.—Taken from cat 91 (Table I, Group 1, p. 376). Ascending degeneration after section of the posterior longitudinal bundle on left side. Note degeneration of fibres on the left side of the area in fig. 3*b*.

If the experiments and anatomical data contained in Chapter III, § 2, be considered, it would seem possible that the cases dealt with in this section demonstrate a secondary ascending connexion of the descending ramus of the vestibular nucleus. As evidence in support of this view are the three cases (VIII, Nos. 18 and 35) where, after lesion of this part of Deiters' nucleus rolling movements to the non-operated side followed. As, however, it was impossible in these three cases to determine positively that there was an ascending degeneration in the posterior longi-

tudinal bundle after lesion of the ramus descendens, with the Marchi method, one is not justified in drawing any further conclusions. Unless we can assume that the axons which ascend from that part of the vestibular nucleus form a synapse with an adjoining group of cells—e.g., in the nucleus triangularis or nucleus raphe—we are unable to explain the exceptional behaviour of the ramus descendens as compared with all other primary centres of the vestibular nerve. In the light of the physiological facts brought forward in §§ 4 and 5 of this chapter, it is interesting that according to Cajal (vol. ii, p. 267) the collaterals from the posterior longitudinal bundle to the fourth nucleus take their origin, without exception, from the *lateral* parts of the posterior longitudinal bundle.

## Chapter IV.—A Centrifugal Bundle which controls the Rolling Movements to the Non-operated Side.

In Chapter II the material of this investigation was considered with reference to its bearing on the supposition of several authors, anatomists, physiologists, and clinicians, that not only the centripetal bundles which control the equilibrium of motion in the horizontal plane form an important part in the posterior longitudinal bundle, but that the tracts which control that function in a centrifugal sense also find a place in this structure. Table II, p. 378, certainly contributes fresh evidence in favour of this supposition. In those animals where a lesion of the ventral part of the mid-brain is associated with circus movements towards the side of the lesion the probability is certainly furnished of the existence of a descending bundle which originates in the region of the posterior commissure. The experiments not only confirm the law of Schiff and Probst ("after hemisection of the posterior part of the optic thalamus circus-movements follow to the side of the lesion"), but they furnish experimental data which tend to prove that in such cases the lesion of a certain group of cells and the consequent degeneration in the extreme mesial part of the posterior longitudinal bundle are responsible for this form of forced movements. The conclusion is therefore arrived at that the maintenance of the equilibrium in the *horizontal* plane is assured by a double system of ascending connexions situated on either side of the mesial line, and also by a descending tract between the posterior commissure and the region of the vestibular nuclei. This system of tracts shows distinct connexions with the nuclei of the ocular nerves, which are quite sufficient to

explain the conjugate deviation of the eyes in the horizontal plane which regularly accompanies the circus movements.[1]

Owing to the descending connexions with the medulla oblongata, the concomitant action of the neck, trunk, and extremities may be regarded as assured. By means of this double system the compensatory movements of the head and eyes are accomplished after unilateral lesion of the tracts, either ascending or descending, which are associated with circus movement and conjugate deviation in the *horizontal* plane of the eyes.

In conclusion, the experiments made in connexion with this investigation are examined as to their bearing on the question of the arrangements for rotatory movement, or locomotion in a plane vertical to the long axis of the animal. Is there an arrangement of tracts similar to that involved in the forced movements already discussed?

Physiologists, anatomists, and clinicians have shown less interest in this problem than in that dealing with the circus movement and conjugate deviation in the horizontal plane. This is partly due to the fact that this particular form of conjugated deviation (Hertwig-Magendie squint) is only rarely met with in pathological conditions, and also because the rolling and allied phenomena seen in physiological experiments are but very imperfectly understood.

Vulpian [159], Schwahn [145], Russell [138], and recently Biehl [21], have proved that as a forced movement or as a forced position it

[1] The conjugate deviation of the eyes and neck is directed, as a rule, towards the same side as the circus movement, but Grasset [66] maintains there are exceptions to this rule. This author observed a case where there was conjugate deviation of the eyes to one side and lateral deviation of head to the other side. He ascribed this occurrence to an uncommon combination of lesion in different tracts. A case which illustrates this better is that reported by Kooyker [83] where a haemorrhage had occurred in the upper part of the internal capsule on the right side. As a result, there was conjugate deviation of eyes to the right and deviation of the head to the left side so long as the symptoms of irritation were present. It must be admitted that besides the destruction of some tracts others were probably subjected to irritative lesions. (Cf. Chapter VII.)

Another very common combination in all classes of vertebrates (cf. 211 and 217, p. 107) is circus movement to one side and rolling movement to the other. This is, of course, easily explained by the peculiar arrangement of the ascending vestibulo-mesencephalic and the descending mesencephalic tracts (fig. 14). This rule also has its exceptions which can be accounted for by an unusual combination of lesion. Thus in No. 108 (cf. Group 11 of the table) the interstitio-spinal tract on one side and the commissuro-medullary tract on the other side are degenerated, while the animal shows a rolling movement to the left side, combined with a circus movement to the same side. In sharks and frogs I found this association of circus movements to one and rolling movements to the other side a very common combination; also in octopods after extirpation of one otolith [110]. It is of interest to note that equally in crustaceans unilateral lesions of the central plexus is associated with circus movement to the intact side and rolling movement to the other side [47].

appears especially after lesion of the restiform bodies.[1] Hogyes [70], and Kubo [84] have noted this form of squint as a reflex phenomenon brought on by certain passive rotations of the head. Hunnius [75], MacGregor [97], and Stewart and Holmes [71], have found it in cases of cerebellar and pontine tumours. Friedberg [60] and Meynert also observed true rolling movements. In diseases of sheep it appears to have distinct diagnostic value [152]. An extensive literature such as there is on the subject of conjugate deviation in the horizontal plane is quite lacking.

The rare occurrence of the skew deviation in the higher organized animals with a combined visual field is explained by Clarke, working in Horsley's laboratory, as a vestigial trace of a former phylogenetic condition where this form of squint was a useful reflex mechanism associated with monocular vision! Where so little is known about the phenomenon and the centripetal tracts controlling it in experiment or in disease, it is not surprising that, so far as I am aware at least, the problem as to whether there exists a tract or centre, the descending degeneration or lesion of which is associated with a rolling movement round the axis of the body and other minor allied symptoms, has not arisen. This problem is embodied in the question as to whether in the present investigation there is any experimental evidence of a descending tract originating from a centre in the region of the posterior commissure which when degenerated is associated with rolling movements and allied phenomena.

The Table II and Chapter II afford information about the tracts which were found to be degenerated in or about the posterior longitudinal bundle after lesion in the region of the posterior commissure. They are: (1) the fine fibred commissuro-medullary bundle; (2) the thick fibred interstitio-spinal tract;[2] (3) the bundle lateral to the posterior longitudinal bundle described by Probst, Economo and Karplus, and van Valkenburg [158]. From the physiological analysis

[1] The author disposes of several extensive degenerations of this body in animals that performed no forced movements.

[2] The interstitial nucleus was recognized to be an anatomical entity in fishes by Fritsch and Mayser before Cajal (1896) described it; the nucleus commissuræ posterioris, lying caudally to the radiation of the posterior commissure, by Darkschewitch. The commissuro-medullary tract was not, so far as I am aware, described until my paper appeared in 1912 [108]. In this paper I described the origin and termination of this tract, and of the interstitio-spinal tract of Boyce and Cajal (1895). The same subject was dealt with in a second paper which was published in 1913 [109]. The existence of the commissuro-medullary tract was, however, strongly indicated by the interesting data collected by Kohnstamm and Quensel [80] on axonal reactions in the commissural region after a lesion of more caudal parts.

of the cases where circus movement was found, it seemed highly probable that the commissuro-medullary bundle is the centrifugal tract controlling this movement.

In this connexion (rolling movements) we have to consider the second and third of the descending bundles especially. If the cases where the rolling movements or some of the allied minor phenomena were maintained for a longer period be picked out, then the Cases 107 and 108, the case of Probst and that of cat No. 3, recorded by Economo and Karplus, stand apart. From the consideration of these cases it was concluded that the interstitio-spinal tract was degenerated on the side of the lesion in the post-thalamic region. Further, in these animals the rolling movements or allied phenomena were always towards the normal side. The question now arises: Is this a simple coincidence or is the rotation dependent on the degeneration of the centrifugal limb of a reflex mechanism for the equilibrium in the plane vertical to the long axis of the animal?

As yet I do not consider that sufficient evidence has been collected to allow of a definite decision being come to on this point, but the question is one well worthy of further investigation.

Only in very localized lesions in the region of the posterior commissure was it possible to localize the probable origin of the interstitio-spinal tract, as the Marchi method in most cases is worthless for recognizing definite cell groups.

Case 108 (fig. 7) afforded evidence for determining the lateral boundary of the origin of this tract, while Case 23 afforded evidence for the dorsal boundary. From such evidence the identity of this nucleus and tract with that described by Cajal is established, while they are definitely differentiated from the nucleus of the posterior commissure and its commissuro-medullary bundle.

The tract lateral to the posterior longitudinal bundle was first described by Probst [124, vol. xxiii, p. 54], and later by Economo and Karplus [78], and Besta [17]. It consists of a bundle of widespread delicate fibres which originate in the prærubral region, and, as shown in Case 108 (not in the figure), appear lateral to the nucleus interstitialis. It does not enter into relation with the third nucleus but descends on the same side latero-ventrally to the posterior longitudinal bundle, terminating in the ganglion tegmenti profundum (Gudden) immediately caudal to the fourth nucleus.

As already stated, I am not prepared either to deny or affirm that this tract has anything to do with the functions discussed in this paper.

I would, however, point out that it is exceedingly improbable that this tract corresponds with the descending tract of Collier and Buzzard [42], since in my preparations none of its fibres descend lower than the pontine region.

A study of the various lesions of the posterior commissure described by the above-mentioned authors and myself, leads to the conclusion that these fibres do not cross the commissure or the raphe. From the direction of the fibres it would seem that they originated in the nucleus intra-commissuralis of the same side, which lies in the middle of the commissure, antero-posteriorly. This nucleus, according to Kohnstamm [80], does not degenerate after hemisection of the cord, but after lesion of the brain-stem. Economo and Karplus [78], however, advance the theory that this tract originates in the corpus mammillare (p. 395, cat No. 3), while also the observations of Probst, Lewandowsky, Flatschek and van Valkenburg [158] seem to lend confirmation to the view that it is part of the tractus mammillo-tegmentalis.

On the whole the results of the present investigation tend to show that a lesion of the nucleus interstitialis (Cajal) is followed by a rolling movement towards the opposite side from the lesion. This direction of the movement is in agreement with the results obtained by v. Bechterew [10] in his experiments on the infundibular region in dogs.

In these cases the fasciculus interstitio-spinalis was found degenerated with such regularity that it seems highly probable that it contains the centrifugal limb of the superimposed vestibular reflex arc dealing with this function. Knoll [79] and Topolanski [155] by electrical stimulation of the region of the posterior commissure caused rolling movements towards the side of the irritation, i.e., opposite to the direction observed in my cases of direct lesion[1].

In this connexion it may be recalled that hemisection of the base of the mid-brain of the frog and fishes causes, according to Steiner, circus movements towards the non-sectioned side; this again is in accordance with our results with section of the posterior longitudinal bundle caudal to the nuclei of the posterior commissure. According to my own experiments on frogs and sharks the accordance between the experiments in lower and higher animals in this structure goes still further, in that also the lower animals, in performing this circus

[1] Pathological observations regarding this matter seem to be wanting. The only case, so far as I know, which was examined with the Marchi method was Case 4, recorded by Roussy [135], where the left eye is described as turned downwards, while the fasciculus interstitio-spinalis was degenerated.

movement, show a tendency to roll to the side of the lesion (cf. Flourens and Baudelot). A fundamental difference in these groups of animals lies however in the fact that in the lower ones no lesion oral to the commissura posterior brings about forced movements, whereas in the higher animals they do, the direction of these movements being inverse to that caused by a lesion of the posterior longitudinal bundle. Physiologically speaking, we have probably to deal here with a very old phylogenetic arrangement. At least it is interesting to note that Wallenberg [164, p. 393] came to the conclusion, on purely anatomical grounds, that the ventro-median part of the thalamencephalon of vertebrates subserves octavo-lateral functions, and is phylogenetically of far older date than the dorso-lateral part, which represents a recent acquisition and is associated with somatic sensory impulses.

The literature on the effects of the prosencephalon on conjugate deviation in the lower animals is very scanty and unsatisfactory. Boyce and Warrington [29] observed that in birds stimulation of the lateral ventral part of the fore-brain, or the origin of the strio-mesencephalic tract, is associated with conjugate deviation of the head and eyes to the other side. In fish, amphibians, and reptiles, both the free movement of the head and neck in the horizontal plane and the cerebral centre for this movement are probably too poorly developed to allow of the demonstration of conjugate deviation by electrical stimulation of the striate connexion of the posterior commissural nucleus. It has been shown above that in these animals, as in birds, the removal of one cerebral hemisphere does not produce the circus movements or conjugate deviation towards the side of the lesion seen in all the higher vertebrates (cf. Chapter VI).

## Chapter V.—Conclusions and Discussion of Results.

### § 1.—*Plan adopted.*

The main object of this paper is to attempt to analyse the complicated vestibular system with its ascending and descending connexions by physiological and anatomical methods. Since it was demonstrated in a former investigation that a lesion of the posterior longitudinal bundle is primarily associated with two forced movements, it seemed possible that a study of these movements might help to elucidate a number of fundamental points, about the structure and function of Deiters' region and the posterior longitudinal bundle formation, where

a purely anatomical analysis fails.[1] Thus Flechsig, v. Bechterew, Ziehen, and particularly Hösel [72] have drawn attention to the fact that some strands in the medulla and the posterior longitudinal bundle are the first to become myelinated. The presence of the posterior longitudinal bundle as a separate tract even in the lowest vertebrates, including the eyeless mammals, is but imperfectly understood. Further, it has long been known [116] that in embryonic rays, as soon as locomotion is possible, a fine puncture involving the posterior longitudinal bundle region causes vehement rolling movements so long as the umbilical cord permits.

These facts led us to adopt the phenomena observed after a localized lesion of the posterior longitudinal bundle formation as a starting point for such an analysis.

## § 2.—*Forced Movements and Semicircular Canals.*

In this analysis the vestibular nuclei must be considered as a system of cell masses, each one of which controls the condition of equilibrium in one of two different planes,[2] and is provided with separate ascending and descending connexions.

Flourens [57], Spamer and particularly Breuer [31] and Kubo [84] have proved that irritation of any semicircular canal elicits movements in the plane coinciding with the canal experimented upon. Breuer and Kubo lay stress upon the fact that movement of the labyrinthine fluid towards the ampulla causes reflexly a conjugated movement of the eyeballs, in the direction opposite to that caused by movement of the fluid from the ampulla. Ewald [52] equally insists that each labyrinth rotates the head and eyes to either side. Each canal therefore should have a double representation in Deiters' complex. Hence in the schematic representation of the results of this investigation (fig. 14),

[1] Although I personally prefer the Marchi method (Busch's modification) to any other, even to the combination of the Marchi and Nissl methods, which is increasing in popularity, yet I consider it inadequate to decide such questions as to whether the vestibular fibres terminate in Deiters' nucleus proper or not. In this region one is particularly liable to fall a victim to false conclusions, since any lesion of the posterior brain cavity, even the removal of the bone, may bring about slight degenerations in the cell masses. Here therefore is an opening for anatomo-physiological research, based upon a large number of experiments.

[2] In this communication the cell masses and ascending connexions which control forced movements in the third plane, that is the plane coinciding with the long axis of the body vertical to the horizontal plane and in which tumbling and staggering occur, are not discussed.

a close functional relation is anticipated between the horizontal canal and Deiters' nucleus (triangular part), together with Bechterew's nucleus, and also between the anterior vertical canal and the descending branch of the nucleus vestibularis, together with the dorsal part of Deiters' nucleus. Should this relationship prove to be anatomically correct it does not of course indicate that the two forced movements, conjugated deviation and reflex nystagmus, coincide with the planes of the canals. It is almost certain that the anatomical arrangement of the skull and the customary mode of progression of the animal will also play a part. The latter factor will undoubtedly influence all reflex phenomena dependent on the vestibular system [32]. It may also be responsible for the prevalence of rolling movements after labyrinthine lesions in most vertebrates[1] for, according to Breuer [31], the mobility of those animals is most dependent on equilibration, in the plane vertical to their long axis. Biach and Bauer [19] came to a similar conclusion, a result of their own experiments and those of Marburg and Bing on the ascending spino-cerebellar tract. In my schematic diagram (fig. 14) no reference is made to the otoliths which are probably, as Breuer [31], Kreidl and Kubo [84] believe, connected with the perception of linear movement, while the semicircular canals are associated with the perception of angular movement. Both organs are evidently closely associated in their action, and there is no doubt that hardly any movement of the head is associated with the stimulation of one semicircular canal only (Ewald [51]).

### § 3.—*Character and Mechanism of the Forced Movements, in Lower and Higher Animals.*

Although in the anatomical and physiological analysis of the posterior longitudinal bundle formation dealt with in this paper, parallels have more than once been drawn between the two forms of forced movements, it must be borne in mind that, from a physiological standpoint, the character of these movements, circus and rolling, is very different. The rolling movements when present and well developed are mostly characterized by their vehement nature, while the circus movements are

[1] An exception to this rule is found in turtles, where the shape of the carapace prevents any falling to the side. In these animals even lesions in the region of Deiters' nucleus do not apparently cause true rolling movements (Fano, Bickel [20]).

quieter and more deliberate. Where both are present in a medullary lesion the rolling movements are nearly always the more conspicuous, in fact it is only after the rolling movements have been partly compensated for that the tendency to go to one side manifests itself; if both are present in thalamic and quadrigeminal lesions, the circus movements are far more pronounced.

Usually, owing to the peculiar arrangement of the ascending and descending tracts in the posterior longitudinal bundle formation, subserving these functions, circus movement to one side is accompanied by rolling movements to the other side. This rule has in a large number of experiments its exceptions, owing to peculiar situation of the lesion. On this ground, as on many others, Brown-Séquard's and Prévost's doctrine on the identity of the two types of forced movements can no longer be maintained. This theory has until very recently found supporters amongst physiologists.

In a physiological sense, there are even more points of difference between the two forms of forced movement. Goltz has shown that after bilateral section of the cerebrospinal stem in the frog, the hind part of the brain which is still in connexion with the vestibular apparatus is sufficient to maintain equilibrium in the vertical plane, vertical to the long axis. If the animal be laid on its side it returns to the normal position, executing a rolling movement. From this the conclusion seems inevitable that for the maintenance of the equilibrium in the plane vertical to the long axis of the animal the peripheral reflex arc in the frog (anterior vertical canal—Deiters' complex —descending tracts into the spinal cord) is endowed with a certain amount of autonomy. It has not yet been proved that the lower vertebrates have like the higher a mesencephalic reflex arc in the posterior longitudinal bundle formation, which, with the medullary reflex arc, dominates the compensatory movements in the vertical and horizontal planes, but it is possible that such an arc does exist. It is noteworthy that in the lower vertebrates the direction of the forced movements does not change when the lesion extends to the region of the posterior commissure.

As to the higher animals, attention may be here drawn to the fact that both the peripheral reflex centres (for both types of forced movements) are provided with spinal axons, but far more important in one case than in the other. It may be recalled that the axons from Deiters' nucleus, as well as those from the nucleus interstitialis, descend into the sacral region, while from the Bechterew nucleus and from the nucleus commissuræ posterioris, they rarely reach beyond the cervical

region.[1] If these physiological and anatomical differences be kept in view, and also the opinion urged by Breuer that the equilibrium in the plane vertical to the long axis of the animal is extremely delicate, more especially in quadruped vertebrates, and therefore in need of constant adjustment, it is evident that the different characteristics of the forced movements after cerebral lesion appear in a new light. The fact that distinct rolling movements are never observed after cortical lesions of the cerebral hemisphere supports the view taken by Hughlings Jackson, that the cerebellum acts as a reinforcing organ for the function of gait and station represented in the mesencephalon, independently from the pyramidal tracts. Prus [127], in his experiments, demonstrated that the co-ordinated running about movements induced by stimulation of the lenticular nucleus are not interfered with by section of the pyramidal tracts.

Further the experiments of Mingazzini [101], Probst [123], Karplus and myself, all furnish evidence in favour of the view that the pyramidal tracts have little influence on locomotion in the quadruped.

The readjustment of the normal position in a plane vertical to the long axis of the animal requires an instantaneous activity of its reflex arcs. I hold that the tonic influence of the cerebellum [Luciani 95] by virtue of its relationship with the vestibular and kinæsthetic impulses (Jelgersma, Lewandowsky, and Lusanna's doctrine) is an indispensable factor. Its absence in cerebellar disease has lately been clearly demonstrated by Babinski's adiadokokinesis. Thomas [154] and Cajal rightly insist that the reflex arrangement, which brings about instantaneously the compensatory movements that ensure the maintenance of the equilibrium during any voluntary movement, largely depends on vestibulo-cerebellar connexions and the cerebellum. Whether, as Bolk [26] and van Rynberk [139] think, this function has a definite localization in the cerebellar lobes is uncertain, but it seems rather probable, since the afferent tracts are not spread diffusely over the entire organ. Magnus and de Kleyn's labyrinthine reflexes depend probably exclusively on our peripheral reflex arcs, which, by virtue of the transverse section in the mid-brain, have acquired a certain amount of autonomy.

[1] It is also very interesting to note the fact recorded in the paper of Magnus and de Kleyn [98] that rotation of the head influences reflexly the innervation of the extremities and consequently their position. Lateral deviation in the same mammals has, on the other hand, no apparent influence.

### § 4.—*Forced Movements after Lesion of Deiters' Complex and Ascending Connexions.*

As the result of experiments on different parts of Deiters' complex, the following conclusions have been come to. As regards locomotion in the horizontal plane:—

(1) Circus movement *towards the affected side* is seen after lesion of the triangular part of Deiters' nucleus and after destruction of its *crossed* vestibulo-mesencephalic tract, originating in this nucleus.

(2) The circus movement, or rather conjugate deviation, is *towards the non-affected* side after lesion of Bechterew's nucleus and the *homolateral* vestibulo-mesencephalic bundle which originates in this nucleus.

It is therefore physiologically demonstrated that there is a functional difference between these nuclei and also between their ascending and descending connexions.

As regards the locomotion in the vertical plane, vertical to the long axis of the body, experiments on the ramus descendens of the vestibular nucleus and on the magno-cellular dorsal portion of Deiters' nucleus, or Deiters' nucleus proper, lead to forced movements in this plane.

(3) Rolling movements *towards the affected side* are seen after lesions of Deiters' nucleus proper, and the lateral horn of the posterior longitudinal bundle *of the same side* or tractus vestibulo-tegmentalis lateralis, that originates in that nucleus.

(4) Rolling movements *towards the non-affected side* appear to occur after lesion of the descending branch of the vestibular nucleus, and also, it appears, in some cases after a local lesion in the mesial portion of the lateral horn of the posterior longitudinal bundle on the same side. This bundle, if proven to exist, may probably be termed the tractus vestibulo-tegmentalis medialis.

From these anatomical and physiological facts we are inclined to infer that the horizontal and anterior vertical canals of each side are doubly represented in the vestibular complex of that side.

### § 5.—*Localization of Tracts in the Posterior Longitudinal Bundle Formation.*

In fig. 14 the relative positions of the six tracts which lie in the posterior longitudinal bundle formation and control the forced

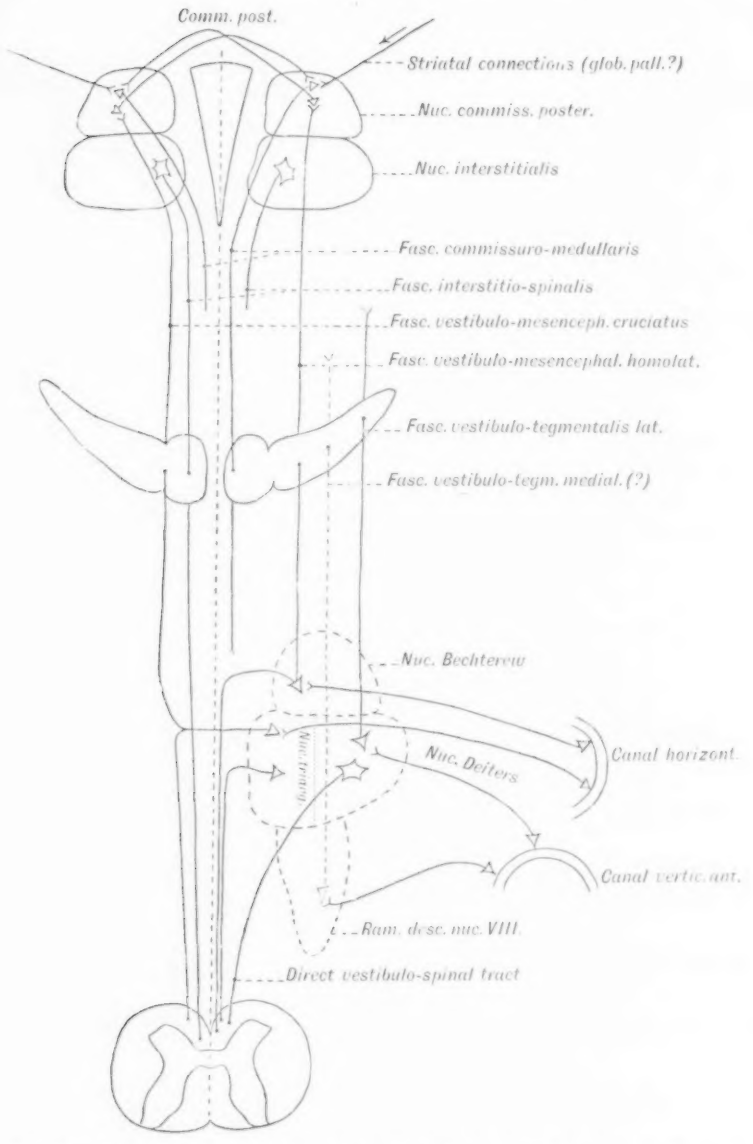


FIG. 14.—Schematic representation of tracts and centres, discussed in this paper. According to Bernheimer, the hemispheral connections with the nucleus commissurae posterioris should be exclusively crossed ones.

movements in the two planes[1] are demonstrated. In the innermost segment lies the finely granular tractus commissuro-medullaris and the coarsely granular tractus interstitio-spinalis. The rest of the posterior longitudinal bundle formation consists exclusively of centripetal tracts which ascend from Deiters' complex. The ascending fibres lying in the posterior longitudinal bundle are arranged in the following manner from within out: First is the crossed tract which ascends from the nucleus triangularis; next is the homolateral vestibulo-mesencephalic tract which ascends from Bechterew's nucleus. The tractus vestibulo-tegmentalis lateralis, which is an ascending tract from Deiters' nucleus proper, lies in the most lateral part of the posterior longitudinal bundle, while a tractus vestibulo-tegmentalis medialis, possibly originating from the ramus descendens, is supposed to lie mesial to it.

Generally speaking, therefore, the centrifugal fibres lie in the cat at the inner margin of the posterior longitudinal bundle. Next in order are the crossed fibres, and then the homolateral fibres (this agrees with Wallenberg's findings in birds). The bulk of the fibres of the posterior longitudinal bundle formation, oral to the vestibular complex, is therefore composed of tracts carrying centripetal impulses associated with the equilibrium of motion in the two principal planes. Since the centrifugal tracts which participate in the posterior longitudinal bundle formation appear to be equally associated with locomotion in these planes, the supposition advanced by Cajal, Spitzer [149], Kohnstamm [81], Hogyes, Marina [100], and others, that the posterior longitudinal bundle formation in the brain-stem and medulla is primarily associated with reflex locomotion in these planes, together with allied compensatory movements necessary for equilibration, seems justifiable.

The only nerves which besides the vestibular have an important reflex action on this system are the optic and acoustic (less so the olfactory) nerves; all three are situated orally to the vestibular complex. It is not surprising, therefore, that, as the researches of Wallenberg, Fraser [59], Probst, and Kohnstamm have shown, there are probably no centripetal fibres below the vestibular complex at all.

When the results of a series of lesions made in the posterior longitudinal bundle formation from the vestibular complex to the posterior commissure are considered from the physiological standpoint, two facts

[1] It will be shown, in a subsequent paper, that the forced movements in a plane vertical to the longitudinal axis of the animal, such as staggering and tumbling, are also controlled by similar nuclei and tracts. Wallenberg's basal olfactory bundle and its fibres joining the posterior longitudinal bundle and Tschermak's (from the central median nucleus?) ascending fibres in the same fascicle are not taken into consideration in this study.

become evident. First, the forced movements caused by ascending degeneration of the vestibulo-mesencephalic and vestibulo-tegmental tracts are of correspondingly shorter duration the nearer the lesion is to the posterior commissure. As a matter of fact, it has also been noted by v. Bechterew [12] and Lewandowsky [89] that forced movements after mesencephalic lesions are of a less pronounced character than those seen after lesion of the posterior longitudinal bundle formation, and of a far less pronounced character than those occurring after lesion of the vestibular complex.

This I formerly held to be due to the fact that the degeneration of the nerve-sheaths progresses at a certain rate, and the stimulation necessary for the production of those forced movements, being dependent on this degeneration, is naturally more transient the nearer the lesion is to the end station. It is interesting to note that, according to the statement by Kohnstamm and Quensel [80], the tigrolytic action is better marked the nearer the lesion of the axis-cylinder is to the end station. Since, however, I got convincing proof, from experiments in the thalamic region, that the forced movements of a longer duration are probably always due to a deficiency of the nerve influences on the one side and the unantagonized action of the analogous structures on the other side, a simpler explanation offers itself. It is this, the functional arrangement of the ascending vestibular system is such that the further the lesion is from the vestibular region the more easily and completely does the compensatory mechanism step in. This holds good particularly for rolling movements. We are not, however, prepared to give anatomical data in support of this generalization.

Secondly, it appears evident that in the higher mammals in a series of lesions, from below upwards, the direction of both forced movements changes abruptly as soon as the region of the posterior commissure is reached. In the lower animals (fishes and reptiles), on the other hand, forced movements are absent after lesions lying higher in the cerebrospinal axis than that commissure.

I held formerly that this change of direction of forced movements in higher mammals was due to the fact that the major irritation which is dependent on the ascending degeneration of the above mentioned tracts, and which acts by means of the posterior commissure on the heterolateral reflex centre, is put out of action, while the weaker stimulus of the descending degeneration of the commissuro-medullary and the interstitio-spinal tract comes into force. Later observations in lower animals led to the belief that in these simpler creatures the ascending vestibular system stops short in the mesencephalon; where, as in the higher ones, the superimposed reflex centres are linked to newly acquired neurons in the striate body, thalamus and pallium (Ariens Kappers [3]). Hence in reptiles ablation of a cerebral hemisphere causes no circus movement

to the side of lesion, nor does faradic stimulation of the striate body cause conjugate deviation of head and eyes to the other side, as it does in all higher vertebrates, including birds.

## Chapter VI.—Forced Movements after a Lesion in the Mesencephalic and Thalamic Regions; the Superimposed Reflex Arc and its Afferent Systems.

As regards the constituents of the posterior longitudinal bundle formation, fresh evidence is afforded by the former chapters in support of the view taken by other workers that this bundle contains centrifugal as well as centripetal bundles, and further arguments are brought forward that these centrifugal tracts control the equilibrium of movement in two planes.

It appeared probable that the commissuro-medullary bundle is the carrier of the centrifugal limb of the superimposed reflex mechanism concerned with the circus movements, while the interstitio-spinal tract is considered the centrifugal one for the rolling movements.

In the controversy on the anatomical side of this subject, between Cajal [40] and de Lange, as to the mesencephalic descending fibres passing into the posterior longitudinal bundle formation certain statements made by both authors may be taken as correct. For example, Cajal describes a strand of fibres passing downwards from the interstitial nucleus in the innermost portion of the posterior longitudinal bundle, while de Lange [86] describes a similar strand of descending fibres in the same part of the posterior longitudinal bundle, but shows that it originates in the nucleus of the posterior commissure. As we have seen in Chapters II and IV, we deal here with two different tracts, each having its own origin and termination, the fibres from the interstitial nucleus passing far down into the cord, while those from the nucleus of the posterior commissure do not extend beyond the medullary region. Arguments are also brought forward to prove that the two tracts subserve different functions. From a study of the results following different lesions in the hypothalamic region and mid-brain, it would appear that forced movements which persist, mostly occur when the region of the nucleus interstitialis and the nucleus of the posterior commissure is injured. In such cases the tracts just described are more or less degenerated.

With these facts to go on one is led to a different conclusion from that arrived at by Boyce [28], who, in discussing the forced movements

and positions, observed after similar lesions, remarked, "It would of course be difficult, with the slight knowledge before us, to attempt an explanation of these phenomena": Probst's similar opinion was expressed in 1900 [124].

Sufficient advance has been made in recent years in our knowledge of the minute anatomy of the brain, thanks to the London, Vienna, Paris, Frankfort, Madrid and Amsterdam[1] schools of anatomy, to ascertain some details of the anatomical structure of both the peripheral and superimposed vestibular reflex arcs. Two peripheral arcs on either side may deal with the compensatory movements in both the horizontal plane and the plane vertical to the long axis. Ascending fibres pass from those double systems to the mesencephalic or hypothalamic nuclei. The arrangement of the fibres, moreover, which pass to those nuclei from the posterior commissure and the cerebral hemisphere is such that a lesion of the nuclei, or of the region immediately oral and lateral to them, is followed by a change in the direction of the forced movements.

The question now arises, have we sufficient anatomical knowledge to trace out accurately the course of these secondary ascending vestibular fibres into the mesencephalic nuclei? It must be frankly admitted that the present methods for staining medullated nerve-fibres are inadequate.

In the case of rolling movements it is even more difficult to demonstrate a complete reflex arc than for circus movements. In the schematic drawing appended the vestibulo-mesencephalic tracts, which control the circus movements centripetally, terminate near the posterior commissural nucleus. So far, my efforts to trace the vestibulo-tegmental tract up to its nodular point have failed, although the nucleus interstitialis has been demonstrated, as far as this physiologically seems possible, as controlling the rolling movements centrifugally. It must, however, be remembered that the Marchi method, which was used, is only effective with myelinated nerve-fibres.

In order to judge by means of a method that brings the non-medullated nerve-fibres to evidence, about the anatomical connexions of the commissural nuclei (nuc. commissur. post. and nuc. interstitialis), I have, with Dr. Bok, carefully examined frontal and sagittal series of sections through chicks' brains, stained after Cajal's silver method. It was easy to confirm Cajal's statement

[1] Personally I feel particularly indebted to Dr. Ariens Kappers for his permission to use his private anatomical library and that of the Dutch Central Brain Institute, and to Prof. C. Winkler, and also Dr. van Valkenburg, for having more than once looked into my series of specimens, and to all of them for having given useful suggestions.

that the majority of neurites descend into the posterior longitudinal bundle, but besides that we found not rarely the axons take a direction towards and into the posterior commissure (ventral division). We saw no axons take an oral direction, but convinced ourselves that the dendrites of a good number of cells of the nuc. commissuræ posterioris are directed towards the oral and ventral parts. This suggests accepting the theory, defended by Tretjakoff and other anatomists, that the dendrites grow out towards the side from which the impulses arrive—that a good number of centrifugal striatal connexions exist in the chick at least that innervate the nuclei in question.

For the anatomical details of the mesencephalic nuclei themselves I must refer to the masterly description given by Ramon y Cajal [40] and to the work of Dejerine [44], who considers that they belong to the ganglia of the central grey matter. In my own investigations I have found, even in selachians, the characteristic large cells of the interstitial nucleus which spread over a large area, and the more definitely localized small-cell nucleus of the posterior commissure.

Passing next to the consideration of the physiological significance of the parts oral to those nuclei, we find that we must confine ourselves to the higher vertebrates, since only in this class does a lesion of the mesencephalic nuclei and the tracts cephalic to them cause forced movements at all, the direction of the movement being opposite to those associated with unilateral lesion of the posterior longitudinal bundle. In this connexion it is interesting to find that all authors are in agreement: in fish and amphibians (Steiner [153, p. 83]), reptiles (Fano [53] and Bickel [20]), and birds, ablation of one cerebral hemisphere is not associated with the development of forced movements. My own experiments, which deal particularly with cats, are in complete agreement with those of Schiff [144], who stated that no local cortical lesion is followed by circus movements which continue for any length of time. A lesion of the deeper parts, such as the striate body or the lateral parts of the thalamus, is, however, followed by circus movements, and conjugate deviation of the eyeballs towards the side of the lesion. This condition may persist for a longer period. It is interesting to note that the circus movement towards the side of the lesion is usually accompanied by a slight rotation round the bodily axis towards the non-operated side. This fact was also noted by Prévost [122]. From an examination of my own material I find in these cases a strand of degenerated nerve fibres, which runs in a latero-median and slightly antero-posterior direction through the external medullary lamina, spreads out in the field of Forel, and disappears near the frontal part of the red nucleus (figs. 15*a* and 15*b*).

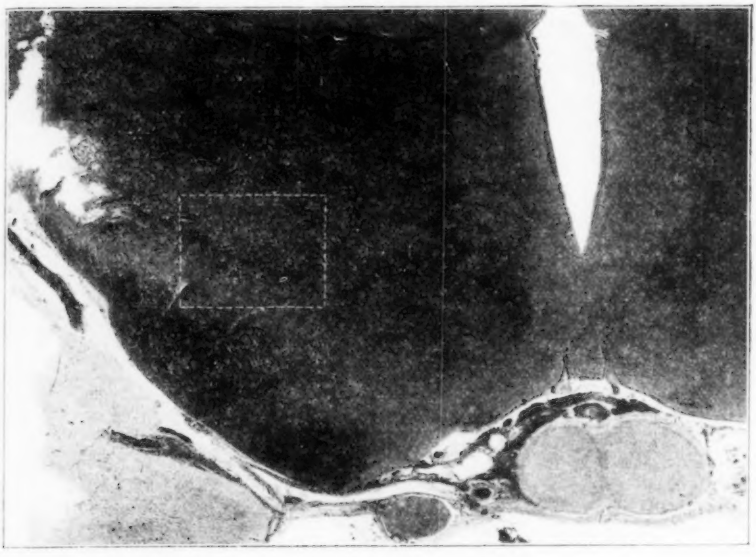

Fig. 15*a*.

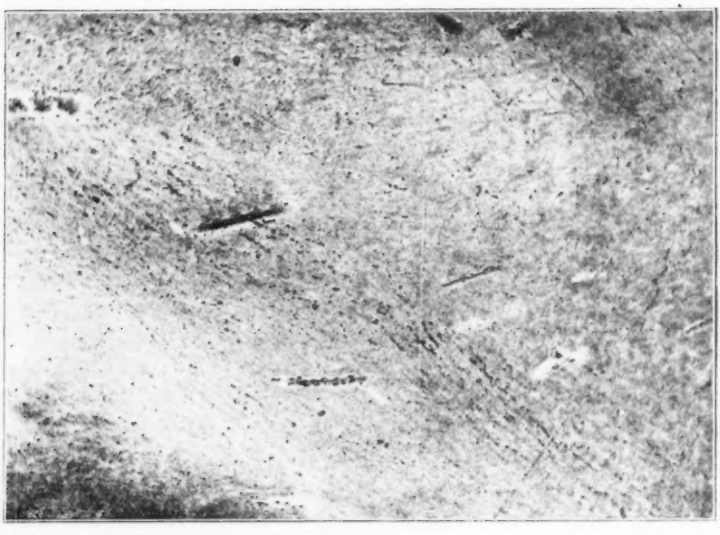

Fig. 15*b*.

FIGS. 15*a*, 15*b*.—Cross sections from cat 186.

Fig. 15*a*.—Region of the lesion. Destruction on the left side of the ventral part of the striate body.

Fig. 15*b*.—Magnified portion of fig. 15*a*. Note degenerated strand of fibres in the lamina medullaris externa.

This strand of fibres lies therefore in the same region in which Dejerine [45], Probst [125], and Roussy [135] find that a large number of fibres disappear after lesion of the lateral parts of the optic thalamus.

The first question now is where do those fibres go to?

It is interesting to note that Sachs [140], working in Sir Victor Horsley's laboratory, reported the case of a rhesus, where the lesion lay in the external medullary lamina, and which showed a similar strand of degenerated nerve-fibres. This author believes that those fibres terminate in the red nucleus. From the evidence already discussed, it seems to me more probable that they terminate in the nucleus of the posterior commissure, and, from Bernheimer's experiments, possibly in the interstitial nucleus of the opposite side. This view is further supported by another case reported by Sachs in which the lesion was in the field of Forel; the same bundle of fibres was degenerated, while some fibres in the posterior longitudinal bundle of the same side also showed degeneration, proving that the interstitial nucleus (at least cells, from which the posterior longitudinal bundle fibres originate) was involved in the lesion.

Where does this bundle of fibres described by Sachs [140] and myself originate?

Up to the present time no conclusive evidence on this point has been furnished by our experiments. At the same time I make the suggestion that their origin lies either in the globus pallidus or in the putamen. This theory is suggested by the fact that in none of my cases of lesion involving the cortex alone were these fibres found degenerated, but only when the deeper parts such as the striate body or the lateral parts of the thalamus were involved. It is further supported by the work of Sachs [140], who succeeded in tracing a thalamo-fugal tract, lying in the same situation and following the same course, from the external medullary lamina to the globus pallidus. The data afforded by the pathological cases discussed in Chapter VII, together with the anatomical data supplied by v. Bechterew [11], Ariens Kappers [3] and de Vries seem also to support this theory.

As regards the physiological significance of this bundle the experiments of Horsley, Sachs and Clarke [41] appear to speak in the same sense. They tend to prove that faradic stimulation of the posterior third of the lateral nucleus thalami, that is the region in the immediate neighbourhood of the external medullary lamina, causes deviation of head and eyes to the opposite side. My observation quite fits in here. Section of the bundle causes circus movements and conjugate deviation

to the side of the lesion. Turning to the records given by other workers I find no arguments against my view in the cases given by Probst [125] and Roussy [135]. The older work of v. Monakow [104] and Mingazzini [101] is not suitable for application of this problem, since the brains were not examined by the Marchi method. In some of the older work by Ferrier and Yeo [56] dealing with suboccipital lesions, and in one of Schäfer and Horsley's experiments [142, Case 6], observations of forced movements occurring after lesion of the region under discussion are recorded. These movements consisted of conjugate deviation to the side of the lesion, falling to one side, or rotation of the head towards the uninjured side.

It is now interesting to see whether any of the old ablation or stimulation experiments, carried out when the present anatomical knowledge had not been arrived at, serve to confirm or deny the views put forward in this paper. The experiments by Adamuk [2] and Topolanski [155] are extremely interesting since the gross resections of the brain-substance indicate fairly accurately that our commissuro-medullary and interstitio-spinal tracts, and also the ascending fibres of the posterior longitudinal bundle, are the elements the destruction of which destroys the co-ordinated ocular movements induced by electrical stimulation of the brain-stem.

So easily were those movements elicited even with slight currents that Knoll [79] suggested that a good many of the results of the stimulation experiments of the cerebral cortex really depended upon current loops [cf. Mott, Schuster and Sherrington, 105]. It will be recalled that Ferrier [54], Schäfer [142], Horsley [14], Beevor and Vogt successfully elicited conjugate deviation of the head and eyes by stimulation over a large frontal area, while Bernheimer [15] and Levinsohn got the same results by stimulating other areas.

From the clinical point of view Landouzy [85] and Grasset long ago pointed out that in disease of the hemisphere conjugate deviation of the head and eyes towards the lesion is due to the paralysis of those structures which on faradic stimulation cause conjugate deviation towards the opposite side. Whether the voluntary impulses from the cerebral cortex, which are associated with forced movements or conjugated lateral movements of the eyeballs, are at all times transmitted through the centrifugal limb of the superimposed reflex arc, as described in Chapter III and in this chapter, must in the meantime remain an open question. It may be, however, admitted that the results of Munk [106] and Levinsohn [88] support this suggestion. Further, in the

light of our results, it seems highly probable that Bernheimer [15] is right in believing that these impulses must travel along paths situated on the ventral side of the sylvian aqueduct.

My experiments, taken in conjunction with those of Horsley and Sachs, lead to the supposition that the inner portion of the lenticular nucleus and its connexions with the nuclei of the posterior commissure are associated particularly with the conjugate deviation of the head and eyes towards the side of the lesion in the case of destruction, and towards the other side with electrical stimulation. Also Ferrier [54] found in the genu of the striate body a centre, electrical stimulation of which caused conjugate deviation from the side of stimulation.

Clinical and anatomical observations also tend to corroborate this view. Uhthoff [157], in his interesting article dealing with a series of anatomical lesions in the cerebral hemisphere in man which had caused conjugate deviation during life, describes the lentiform nucleus, claustrum, internal capsule, optic thalamus, and caudate nucleus as being most frequently involved. Prévost and Broadbent had made similar remarks before. Hösel [72] also found that one of the first tracts to become medullated is that which connects the region anterior to the red nucleus with the globus pallidus.

All this independent evidence seems to urge the necessity for a further investigation on the relationship between strial and cortical influx and the conjugate deviation of the head and eyes, from the newly acquired points of view.

## Chapter VII.—Conjugate Deviation of Head and Eyes, and Different Forms of Nystagmus in Clinical Neurology. Their Localization Value.

The physiological analysis of the posterior longitudinal bundle formation has undoubtedly an important bearing on the clinical problem, afforded by the conjugate deviation of both eyes in cerebral disease generally, and particularly in pontine disease involving the sixth nucleus. Unless the physiological analysis of this formation be taken into consideration it is impossible to explain the additional conjugate deviation of the heterolateral rectus internus, with the rectus externus of the diseased side in an organic affection of the sixth nucleus. Foville [58], Hughlings Jackson [74], Duval, Wernicke [166], Bleuler [25], Bruce [37], Bischoff, Spitzer [149] and others, accept the view that

the nervous influx for the lateral movement of both eyes descends to the sixth nucleus and ascends to the third nucleus; they also consider that there is a recrossing of the pyramidal fibres dealing with this movement.

Many authors have felt the difficulty of accepting this somewhat improbable supposition, for which there is further no anatomical basis. If, however, the forced movements in the horizonal plane and the closely associated conjugate deviation in the same plane be carefully considered in the light of the above data, it is evident that there is no need to fall back on this theory.

A full discussion on this subject will be reserved for a later communication, but it may be said here that, after a careful scrutiny of the writings, hardly a case is found where there is not a lesion in the posterior longitudinal bundle formation as well as in the sixth nucleus.

If we consider the conjugated deviation [107, p. 216] as a minor degree of circus movement as well as a part of it, it is seen that this conjugate deviation of head and eyes in pontine diseases to the non-affected side is closely related to the circus movement towards the normal side, seen after one-sided lesion of the posterior longitudinal bundle formation between Deiters' nucleus and the posterior commissure in our experiments.

It is quite natural that in primates this forced movement, with conjugate deviation of the head and eyes, associated with pontine lesion, is to a greater extent under the power of the will than in the case of the lower vertebrates, a more or less continuous effort being made to counteract it. In fact, in the monkey it is rare to find a regular circus movement associated with a conjugate deviation to one side. In any case it never amounts to more than a slight circus movement, such as is seen in cats just before the symptom disappears, which passes, leaving a tendency to conjugate deviation of the head and eyes. Even conjugate deviation is overcome in primates with a certain ease. So it is that Munk [106], Ferrier and Yeo, as also Hunnius and Bernheimer, rightly insist that an unwillingness to look to one side must be looked for in the proper cases. Indeed, circus movement and conjugate deviation of the eyeballs in the horizontal plane, e.g., to the right side, and unwillingness to look to the left side, are all different degrees of the same fundamental phenomenon. It is therefore not surprising to find the heterolateral eyeball in pontine disease of man deviated inward, since a lesion of the eminentia teres and the

sixth nucleus by virtue of its vicinity to the posterior longitudinal bundle involves this bundle also. In this connexion the cases recorded by Rickards [131], Wiersma [167], Bristowe [33], Byrom Bramwell [30], Bruce [37], and Hunt should be examined.

It is only in cases of pontine tumour with no involvement of the posterior longitudinal bundle, but affection of the sixth nerve, that the internal rectus muscle of the other side may be expected to act normally. Reference may here be made to the work of Graux [67], Bennet and Savill [141] and others.

Regarding conjugated deviation in disease of the hemisphere, Wernicke's case [166] has long been regarded, in the German literature, as decisive proof that in man the angular gyrus is a special centre for this deviation. Destruction of this centre has long been supposed to cause conjugate deviation towards the side of the lesion, while irritation of the centre is associated with deviation towards the other side. This theory found support in the fact that in monkeys stimulation of the angular gyrus with the faradic current causes conjugate deviation to the opposite side. A careful scrutiny, however, of the anatomical findings of this case and of Prévost's [123] classical work, and Broadbent's cases [34], taken in the light of our observations on the superimposed vestibular reflex arcs, leads to the conclusion that there is considerable doubt on this point (Klaas). In Wernicke's case the third zone of the lenticular nucleus was involved as well as the cortex of the angular gyrus. This part of the striate body can therefore not be discarded as a centre in connexion with which the symptom of conjugate deviation arises.

Stimulation of the human cortex by minimal faradic currents has never, in my experience, been associated with conjugate deviation, nor, so far as I am aware, have Horsley, Krause or Cushing recorded this result. Unipolar stimulation is for several reasons, already pointed out in this paper, unsuitable for this purpose. For the present, therefore, it seems to me that the localizing value of the hemispheral conjugate deviation must remain *sub judice*. At the same time, I think that the ocular symptoms which occur in cases like No. 11 of Oppenheim's series [119] where the lenticular nucleus is involved, are worthy of considerable attention. If, in addition to paralysis of the nucleus abducens of the one side, there are indications of some paresis of the internal rectus muscle of the opposite side, when both are brought into action simultaneously, the condition may be diagnosed as conjugate deviation to one side or as defective movement

to the opposite side. It must not be regarded as a secondary pressure symptom.

It is interesting to note how clinical observations, quite apart from physiological research, have led to the appreciation of the fact that a destructive lesion of the cerebral hemisphere and optic thalamus is associated with conjugate deviation to the side of the lesion, and that a similar unilateral lesion in the pontine region causes the same deviation from the side of the lesion.

Long ago Grasset and Landouzy stated, "Dans les lésions de l'hémisphère le malade regarde ses membres convulsés, s'il y a excitation, et regarde sa lésion, s'il y a paralysie. A partir d'un certain point mal défini, à la limite des parties supérieures et moyennes de la protubérance, la formule doit être renversée." D'Astros [4] writing in 1894, considers it impossible to localize this "reversal point."

As a result of the observations now recorded there seems to me to be little doubt but that this point is situated in the posterior commissure, probably in the nucleus, both in man and in the lower type of mammal exemplified in the cat.

The question of the exact topographical distribution of conjugate deviation in the frontal and occipital regions dealt with by Ferrier, Schäfer, Horsley, Marina [100], and that which is discussed in the controversy between Luciani [96] and other workers, seems to me to be, after what has been said above, only of secondary interest. Regarding cerebellar disease, I may recall the fact, dealt with in Chapter II, that forced movements were never associated with my experiments involving lesions of the cerebellar cortex, or of the dentate nucleus [8].

The question which Bonnier [27], Launois, Chèze and others have attempted to answer as to whether a special Deiters' syndrome can be recognized in pontine disease, also lies outside this paper.

It is quite evident from what has been said regarding forced movements in quadrupeds that very careful distinction must be made in man between deviation in the horizontal plane and falling to a side. As regards the latter phenomenon it seems certain, from the work of Marburg [99], that besides the falling movements towards the medullary lesion the same movement towards the normal side is not infrequently observed. This latter condition is in agreement with the results got in my experiments on the ramus descendens of the vestibular nucleus. For the most recent observations on this subject I must refer to the second case recorded by Wallenberg [161], to the work of Schwarz [146]

and to the case of thrombosis of the posterior inferior cerebellar artery recorded by Goldstein and Baum [64]. It seems, however, to be the general rule in man, as in the cat, that a lesion of the vestibular nerve-roots and of the more oral parts of Deiters' complex are associated with falling to the side of the lesion. This phenomenon of falling to the side must be specially examined in man since the erect posture makes it impossible to bring it quite into line with the condition as it occurs in quadrupeds, where it really is a minor degree of the rolling movements.

From my observations [107, 113] on the direction of the different forms of nystagmus found associated with lesion of the hind-brain which have been confirmed and extended by Bárány [6], there can be little doubt but that the mechanism in such cases is as complicated as that described for the forced movements, and that the two mechanisms are closely related. I will merely recall that some authors (Marburg and Bartels) believe that the rapid and slow jerk seen in vestibular nystagmus have different localization.

In my experiments the slow jerk of the nystagmus accompanying the forced movements and forced position of the eyeballs always took the same direction as that in which the eyeballs were deviated. In lesions of Bechterew's nucleus and the homolateral vestibulo-mesencephalic tract in the posterior longitudinal bundle, the slow jerk of the horizontal nystagmus is directed towards the uninjured side. If the lesion be situated in the right vestibular root and the right Deiters' nucleus proper then the slow jerk of the nystagmus, associated with this condition, accentuated the already existing divergent squint, the right eye being directed downwards, the left eye upwards. Do these facts justify us in deducing diagnostic points for use in localizing the lesion in cases where one-sided nystagmus is present, but where, as is not infrequently the case in subtentorial lesions, forced movements or conjugate deviation are both absent? It seems to me that this is a point worthy of further consideration, but my own experience furnishes no conclusive evidence on the question.

Generally speaking, this anatomical and physiological research tends to show the importance of accurate clinical observation of even slight defects in the co-ordinated ocular movements in brain disease. Some of these lesions and their accompanying symptoms are as follows: A lesion anywhere from the descending ramus of the eighth nerve up to the striate body is liable to cause certain disturbances. In man these disturbances are more commonly in the horizontal plane, and are at

present so little understood that only a rough outline can be given of the pathological conditions which possibly induce the symptoms.

A *destructive* lesion of the posterior longitudinal bundle on the right side of the brain between the vestibular region and the posterior commissure is liable to cause conjugate deviation of the head and eyes to the left side, or else incomplete lateral deviation to the right side. If this symptom occur when the lesion is oral to the posterior commissure it is indicative of an organic destructive lesion on the left side. If there is conjugate deviation of head and eyes to the left side, and an *irritative* lesion, cephalad to the posterior commissure is probable (eventually convulsions of muscles on the left side), the irritative lesion may be localized in the thalamus and striate body on the right side.

If the symptom of Magendie-Hertwig squint (right eye directed downwards, left eye upwards) occur either alone or concurrently with conjugate deviation of the head and eyes, or if there is a tendency to fall or lie down on the right side, then the lesion (if situated in the medulla or truncus cerebri) probably has involved the vestibulary region or the lateral part of the posterior longitudinal bundle on the right side. If this symptom is present where the disease is localized cephalad to the posterior commissure, then, from experimental findings, the lesion is to be localized in the optic thalamus or striate body on the left side. If a destructive lesion is situated in the vestibular or cerebellar regions, and there appears deviation of the head and eyes to one side, for instance the left, we deal either with a conjugate deviation in the horizontal plane to the *left*, or with a condition allied to the rolling movement to the *right*. A careful searching for the Magendie-Hertwig squint (left eye down, right eye up) or a tendency to lie down on one side (the left) or a divergent nystagmus, slow in the sense of the deviation, will enable us to diagnose a condition allied to rolling movements to the right. Since unilateral cerebellar disease is very liable to affect the vestibular nerve and Deiters' nucleus, it is clear why in this type of case there is frequently a tendency to lie down on the diseased side. It is only in cases where the ramus descendens of the eighth nerve is involved that one is likely to get exceptions to this rule.

After what has been said, it need hardly be pointed out that Bruns' symptom of disequilibration in frontal tumour [38] cannot be discussed, unless the above observations be taken into consideration.

In examining for ocular deviation the voluntary and automatic deviation of the eyeballs must be tested separately. Wernicke [166] states that Tiling long ago pointed out that reflex deviation, such

as is seen when a moving object is followed by the eyes, may be demonstrated while voluntary lateral deviation is lacking. Bielschowsky [22] further emphasized the importance of this fact in routine examination. The symptom of "Vorbeizeigen" in cerebellar disease observed by Bárány may, I think, be due entirely to involvement of the vestibular structures. The fact that horizontal nystagmus is never accompanied by a tendency to fall to one side is quite readily understood when the mechanism of the two types of forced movements is taken into consideration.

The observation that a large percentage of deaf people do not suffer from dizziness, as noted by James and Kreidl, and further, that in very young infants sea-sickness does not occur, seems to indicate that there is some connexion between those conditions and imperfect functioning of the vestibular complex, either peripherally or centrally. The experiments of Nagel [118], Bishop Harman [24], Quix [129], Bartels and Rothfeld [132] render it extremely probable that the compensatory movements of the eyeballs in different movements of the head, and also the reflex adjustment of the eyes in vertical and other directions during rotation, are dependent on the labyrinthine reflexes. Where there is, e.g., circus movement or conjugate deviation to the right side, the compensatory deviation to the contralateral side during and after rotation are found absent. Reddingius, Marina [100], F. B. Hoffmann, and Bielschowsky have investigated the question of the reflex adjustment of the eyes in vertical and other directions during ocular movements; these reflexes will probably be proved to be equally dependent on a normal activity of these reflex mechanisms and their conduction by the posterior longitudinal fascicle [cf. Cajal, 40, i, p. 728].

In the case of octopods [110], it has been shown that the reflex adjustment of the eyeball by the otolithic organ is in this animal predominantly homolateral: by this reflex the pupillary slit is maintained in the horizontal position in practically all the positions assumed by the body. A similar condition seems to exist in the python, as here also the pupillary slit is held constantly vertical.

The very delicate muscular adjustment of the eyeballs in the higher vertebrates which is necessary, according to Mulder, Nagel [118], Hering and Bielschowsky, for the localizing of the visual field to the same part in the two retinæ in all changing positions of the head, is probably also a vestibular reflex system; the innate tendency to fuse the two visual fields, even when anatomical or nervous defects exist, also plays an important part. The work of Marina on this subject is worthy of attention.

SUMMARY.

In reviewing this physiological analysis of the vestibulary system and the posterior longitudinal bundle formation, certain facts, both physiological and anatomical, stand out clearly, while other points can only be considered as suggestions or probabilities.

(1) The study of the physiological phenomena observed after lesions of different parts of this system demonstrates that there is a far-reaching differentiation of function in the primary end-stations of the vestibulary nerve. Further, it also shows that the different strands of fibres which connect the vestibular nuclei with the various nuclei in the mid-brain and with the region of the posterior commissure in a cerebro-petal direction may be more accurately analysed.

(2) The principal vestibular nuclei are the following: (*a*) The descending branch of the vestibular nucleus; (*b*) Deiters' nucleus composed of a ventral caudal division, named the nucleus triangularis, and a dorsal magnocellular division or Deiters' nucleus proper; (*c*) Bechterew's nucleus with the nucleus tecti.

(3) Physiological analysis affords a practical method of establishing the existence of important differences in the ascending and descending connexions of the above-mentioned nuclei, and of establishing equally important differences in the functions of the nuclei.

(4) The starting point of this analysis is the fact that an ascending degeneration of the crossed vestibulo-mesencephalic bundle, which forms the bulk of the mesial part of the posterior longitudinal bundle till near the nucleus of the posterior commissure, is always found associated with circus movements to the side of the intact posterior longitudinal bundle. This rule holds good so long as the lesion leaves the other parts of the vestibular systems intact. It is immaterial whether the degeneration of this vestibulo-mesencephalic tract is the result of a cross section of the median part of the posterior longitudinal bundle, or of a lesion of the heterolateral Deiters' nucleus. Experimental evidence tends to show that in the Deiters' complex the nucleus triangularis is the principal origin of this tract (fasciculus vestibulo-mesencephalicus cruciatus).

(5) The degeneration of an ascending tract lying immediately lateral to the crossed vestibulo-mesencephalic tract in the posterior longitudinal bundle formation appears to be equally associated with a circus movement (or rather conjugate deviation) to the side of the normal posterior longitudinal bundle. This tract is further shown to be a homolateral tract originating exclusively in the nucleus of Bechterew,

at least in the oral parts of the vestibular region, and terminating in the region of the posterior commissural nucleus. This bundle may be styled the homolateral vestibulo-mesencephalic fasciculus.

This tract is only partially identical with that described anatomically by Probst [124]. Van Gehuchten [63] in 1904 suggested that the whole of the lateral part of the posterior longitudinal bundle (fasciculus Deiters' ascendens, Lewandowsky, Winkler [169]) consisted of fibres, ascending from Bechterew's nucleus. This origin, for this limited portion at least of the posterior longitudinal bundle, may now be held as proved [cf. 108], as may also the association of its upward degeneration with circus movements or conjugate deviation to the normal side.

Both the circus movements observed after lesion of the homolateral or crossed vestibulo-mesencephalic tracts are associated with conjugate deviation of the head and eyes to the side of the movement, or with loss of lateral deviation of the eyeballs to the opposite side.

(6) According to the notions advanced by Duval, Bleuler, Edinger, Bischoff, Spitzer, Kohnstamm, Bernheimer, Fraser, Wallenberg, Wiersma, and others, the posterior longitudinal bundle represents a combination of ascending and descending tracts, which control the co-ordinated movements of the eyes, head, and trunk, and control or direct the maintenance of the equilibrium of motion. Now, from experimental data furnished by the present investigation, it is seen that after a direct lesion in the region of the posterior commissure of the cat on one side, where the resulting circus movements were directed to the side of the lesion, a descending tract degenerates which lies at the innermost part of the posterior longitudinal bundle of the same side. This tract probably originates in the posterior commissural nucleus. As it stops short in the medulla it is suggested that it may be termed the fasciculus commissuro-medullaris [cf. 108].

(7) Although it is probable that this mesencephalo-medullary tract exists in all the higher organized vertebrates such as selachians, teleosteans, amphibians, reptiles, birds and mammals, it is only in the mammal that a destructive lesion of the nucleus and of its efferent tracts from the striate body is associated with circus movements towards the side of the lesion. In the lower animals a lesion oral to the posterior commissure is not followed by any circus movements.

The anatomical explanation of this fact seems to be that only in mammals are the hypothalamic and commissural nuclei sufficiently connected with the prosencephalon that section of the connexions should be followed by asymmetrical locomotion, as evidenced in circus

movements and conjugate deviation towards the side of the lesion. Further, it is only in mammals that stimulation of certain definite areas of the cortex is followed by conjugate deviation of the head and eyes towards the opposite side. Birds seem to form in this respect a group between the reptiles and mammals. In the prosencephalon of the bird is an area, faradization of which is associated with conjugate deviation towards the opposite side (Boyce and Warrington). The section of the connexions of this area is not, however, associated with any alteration in the mode of locomotion. As regards those cases (cats), where, after lesion of the thalamus and cerebral hemisphere, circus movements towards the side of the (destructive) lesion were observed over a longer period, it was found that there was a tract of degenerated fibres in the lamina medullaris externa. These fibres, which probably emanate from the striate body, pass to the hypothalamic region, where they lose their medullary sheaths. The termination of these fibres, probably in the nucleus of the posterior commissure, can, therefore, not be demonstrated. The circus movement in such cases is always accompanied by conjugate deviation towards the side of a destructive lesion, or in less pronounced cases by loss of lateral deviation to the other side.

(8) Like the circus movements the rolling movements may serve as a guide in working out the anatomo-physiological analysis of the vestibular complex and the posterior longitudinal bundle formation.

(9) After a direct lesion of the complicated nerve-fibres, which help to form the vestibular root, a rolling movement towards the injured side is constantly observed, mostly associated with a skew deviation and conjugate rotation of the eyeballs around their antero-posterior axis. In only one case (rabbit, direct lesion in the caudal part of the vestibular root) were rolling movements towards the non-injured side observed.

(10) In three cases of lesion of the descending branch of the nucleus vestibularis rolling movements towards the normal side were seen lasting over several days. Although this experiment was repeated several times, I failed to localize any distinct ascending or descending connexions from this part of Deiters' complex.

(11) Lesion of Deiters' nucleus proper is found in two cases associated with rolling movements, moderate in character, towards the side of the lesion. From this nucleus the degeneration spreads upwards along a tract which lies in the outermost part of the lateral horn of the posterior longitudinal bundle. A direct lesion of this ascending tract or connexion is also associated with a tendency to roll towards the side of the lesion. This was demonstrated in five cases.

The fibres of this tract appear to end mostly in the tegmentum, although some may be traced to the caudal part of the posterior commissure, where the fibres appear to lose their medullary sheath: it is therefore suggested that it should be styled the tractus vestibulo-tegmentalis lateralis. Its origin is apparently in the medium-sized cells of Deiters' nucleus proper, its termination probably in the interstitial nucleus.

(12) A comparison of the cases where the lesion is situated in the region of the posterior commissure leads us to postulate in that region a centre, probably the nucleus interstitialis, injury of which (or of its afferent tracts from other parts) in the cat is constantly followed by rolling movements to the normal side. The existence of a descending interstitio-spinal tract in the innermost section of the posterior longitudinal bundle in these cases in which rolling movements or, in less pronounced cases, a tendency to fall to the normal side are observed seems to justify this supposition to a certain extent.

(13) The physiological combined with the degenerative method does not afford such ample information as regards the tracts from Deiters' complex to the posterior longitudinal bundle formation of the spinal cord. This is partly due to the irregular form of the collection of reticular cells which give rise to the ponto- or reticulo-spinal tracts. It seems certain that heterolateral descending fibres of the posterior longitudinal bundle do not come from Bechterew's nucleus, although descending homolateral fibres are given off from both Deiters' and Bechterew's nuclei. After experimental lesion of Deiters' nucleus it was not in all cases possible to decide from what cells the heterolateral fibres originate. If the descending connexions of the vestibular structures which control the circus and rolling movements and those of the superimposed mesencephalic structures be compared, the conclusion seems warranted that the descending connexions are far more important in the case of the rolling movements. Relatively few descending fibres which originate in the structures associated with circus movements pass beyond the sixth nucleus.

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# AN EXPERIMENTAL RESEARCH INTO THE ANATOMY AND PHYSIOLOGY OF THE CORPUS STRIATUM.[1]

By S. A. Kinnier Wilson, M.D., B.Sc., F.R.C.P.

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## EXPLANATION OF LETTERING OF FIGURES.

| | |
|---|---|
| AC | commissura anterior. |
| Al | ansa lenticularis. |
| ANR | anterior capsule of nucleus ruber. |
| CE | capsula externa. |
| CGE | corpus geniculatum externum. |
| CI | capsula interna. |
| CIP | posterior part of capsula interna. |
| CL | corpus subthalamicum (Luysii). |
| CR | crus. |
| Figp | internuncial fibres of globus pallidus. |
| Fip | internuncial fibres of putamen. |
| Fl | Forel's lenticular bundle ($H_2$). |

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| | |
|---|---|
| FlNR | ansa lenticularis fasciculi, via Forel's field, to nucleus ruber. |
| Fsl | strio-luysian fibres. |
| Fth | Forel's thalamic bundle ($H_1$). |
| GP | globus pallidus. |
| L | lesion. |
| Lam$_1$ | lamina medullaris lateralis. |
| Ln | locus niger. |
| M | fasciculus retroflexus of Meynert. |
| N II | nervus opticus. |
| N III | nervus oculomotorius. |
| NAm | nucleus amygdalæ. |
| NC | nucleus caudatus. |
| NFl | nucleus of Forel's field. |
| NR | nucleus ruber. |
| OT | thalamus opticus. |
| PCS | pedunculus cerebelli superior. |
| PUT | putamen. |
| V III | ventriculus tertius. |
| ZI | zona incerta. |

## Introduction.

The exact nature and function of the large mass of basal grey matter known as the corpus striatum have hitherto constituted, it is no exaggeration to say, one of the unsolved problems of neurology. Not that the corpus striatum has failed to attract the attention of anatomist, physiologist and clinician: on the contrary, since the days of Willis, it has received its full share of investigation along all the familiar lines. The disturbing element in the matter of research into its functions has been the conflicting nature of the results obtained. Anyone who will take the trouble to read the curiously philosophic text-books of half a century ago would imagine, it is true, that the corpus striatum was an organ as high in the cerebral hierarchy as the cortex itself, endowed with motor functions as elaborate and as detailed. But a change took place when neurologists realized that many of the functions assigned to it were the property of the adjacent cortico-spinal paths, and almost at once it seemed to fall from its high estate and depreciate in physiological significance. Under these circumstances the question of its function became an enigma, and, as a consequence, there was eventually assigned to it a varied assortment of motor, sensory, vasomotor, psychical and reflex functions, no one of which, it is safe to say, has ever rested on unequivocal evidence. To prove the truth of this statement it is only necessary to quote from such acknowledged authorities as v. Monakow, v. Bechterew and Edinger. In 1905 v. Monakow [56] wrote: "Trotzdem seit Jahren zahlreiche Forscher

bemüht sind, die klinischen Folgen von Läsionen im Gebiet des Streifenhügels und des Linsenkerns zu erforschen, und obwohl die Zahl von genaueren Beobachtungen über Herde in jenen Hirnteilen eine ganz stattliche ist (gehören doch Herde verschiedener Natur und Ausdehnung im Vorderhirnganglion zu sehr gewöhnlichen Vorkommnissen), so sind wir heute ebensowenig wie vor 25 Jahren Nothnagel imstande, sichere Kennzeichen einer Herderkrankung in den genannten Hirnteilen aufzustellen." In 1909 v. Bechterew [6] was compelled to say: "Die funktionellen Zustände des Schweifkerns und des Linsenkerns, welche seit jeher unter dem Gesamtnamen Corpus striatum zusammengefasst werden, sind gegenwärtig einer endgültigen Aufhellung noch immer nicht erschlossen. Über die Bedeutung dieser Gebilde gehen die Meinungen der Autoren, welche sich darüber geäussert haben, vielmehr noch sehr weit auseinander." No longer ago than 1911, Edinger [21] wrote: "Es gibt kaum einen Punkt, der so sehr beweist wie weit bisher noch unsere Beobachtungsfähigkeit zurück ist, als der Umstand dass wir bis heute weder von den Funktionen des Corpus striatum noch von den Symptomen etwas wissen, die eintreten, wenn es zerstört oder wenn es gereizt wird. Da ist ein mächtiger Hirnteil, der von enormer Bedeutung sein muss, sonst wäre er nicht von den Fischen an aufwärts vorhanden, ein Hirnteil der bei den Vögeln die Hauptmasse des ganzen Grosshirnes ausmacht, zudem ein Gebilde, in dem ausserordentlich oft beim Menschen Krankheitsherde gefunden werden und doch hat niemals jemand ein Symptom entdeckt, das von ihm ausgeht."

Within the last two or three years, however, the clinico-pathological method, to which we owe some of the greatest discoveries in neurology, has furnished evidence which goes far towards clearing away the obscurity that has surrounded the subject, and at the same time it has enabled us to reach a truer interpretation of the data obtained by experimental research on the corpus striatum, while it has also indicated the lines along which further experimentation must be prosecuted. As has so often happened before, once insight is gained into the function of a nervous organ, much that has hitherto seemed inexplicable becomes plain, and with notable rapidity further data are collected which bear out the new view. Already, in the last year or two, a syndrome of the corpus striatum has been enunciated which, however much it may come to be modified, shows every sign of being corroborated by each accession of fresh evidence, and in any case can fairly be regarded as furnishing the closest approximation to the exact mode of working of that important structure which has up to the present been reached.

## Chapter I.—Historical.

The vicissitudes through which the corpus striatum has passed constitute an interesting chapter in cerebral physiology, affording an excellent illustration of the methods of procedure of early experimenters, and throwing a valuable sidelight on the stages whereby our present knowledge of the working of the encephalon has been attained.

In 1667, Thomas Willis described the corpora striata as "internodes by which the cerebrum coheres with the medulla oblongata," and on account of their peculiar structure attached such importance to them as to consider them the seat of the "sensorium commune." From this position of high significance thus assigned them by the earliest investigators—an inevitable consequence when we remember their prominent appearance on horizontal section—they have never really declined.

In 1740, Swedenborg [74] published his "Œconomia Regni Animalis," a book in which he showed curious insight into cerebral physiology. To the corpus striatum he attached much importance. Thus he says: "The royal road of the sensations of the body to the soul is through the corpora striata, and all determinations of the will also descend by that road." That organ is "the Mercury of the Olympus, it announces to the soul what is happening to the body, and it bears the mandate of the soul to the body." If we translate his somewhat figurative language into present-day terminology, it is clear that Swedenborg had a conception of afferent and efferent paths far in advance of his time, even though it be but the result of a lucky guess on his part, and that if we suppose he included the optic thalamus in the corpora striata, which lie immediately under and "are most immediately subject to the courts of the anterior (superior) regions of the cerebrum," he thereby developed a theory of the function of the basal ganglia in relation to the cortex which has been almost universally held and even yet is not without its bearing on the problem before us.

At the beginning of last century Burdach [12] (1819) showed that the outer aspect of the lenticular nucleus was unconnected with the fibres of the external capsule and held that the appearances suggested that the fibres of that nucleus did not go to the cortex. He concluded that the basal ganglia are in a psychical sense intermediate between the brain-stem and the cortex, controlling the one and being subsidiary to the other.

Apparently the earliest definite experiments on the corpus striatum were those conducted about the year 1820, by Flourens [26], who failed

to obtain any movements in the rabbit by stimulation of the ganglion. "Je piquai d'abord, dans tous les sens, et j'enlevai ensuite en totalité, par tranches successives, sur un lapin, les corps striés et les couches optiques: nulle agitation n'accompagna cette double épreuve." He failed also, somewhat curiously, to obtain any movements by stimulation of the cortex, and declared that "les hemisphères cérébraux ne sont point susceptibles d'exciter immédiatement des contractions musculaires."

Magendie [49], however (1841), obtained diametrically opposed results. By mechanical stimulation of the nucleus caudatus with a needle he was unable to elicit movement. "Voici le ventricule latéral droit ouvert, la voûte et le septum lucidum enlevés: le corps strié parait au fond de la plaie. Je pique ce corps avec une aiguille enfoncée d'arrière en avant: l'animal conserve toute son impassibilité. C'est en vain que je transperce le corps strié du côté gauche: les résultats sont toujours négatifs." By destroying the corpus striatum on both sides, however, the same experimenter obtained leaping forward of the animal as by an irresistible impulse. It should be stated that the majority of his experiments were on rabbits. "Ainsi, par exemple, je vais couper et extraire les corps striés: vous allez voir l'animal courir en avant comme emporté par une impulsion irrésistible. Il vient en effet de partir comme un trait: je suis obligé de le retenir, et vous voyez qu'il conserve l'attitude de la fuite." And again: "Je viens d'extraire un des deux corps striés: rien encore de modifié dans les mouvements. J'enlève le second corps strié; voyez comme l'animal cherche à fuir. Je ne veux pas le laisser libre, car il irait se briser la tête contre le premier obstacle qui se trouvait sur son passage."

Magendie was of the opinion that movements in a forward direction were under the influence of the cerebellum, while backward movements were controlled by the corpus striatum: if, therefore, the latter were destroyed, the animal should run forward, owing to uncontrolled action of the cerebellum. It is certain from the technique of Magendie that the white matter adjoining the corpus striatum was implicated in the experimental lesions, and their value is thereby discounted.

Longet [45] (1842) dismissed the theory held by Willis as one without any foundation, but admitted his inability to advance another more plausible. He experimented on rabbits, removing first the cerebral hemispheres and then the corpora striata, but failed to obtain Magendie's results, and concluded that "la force motrice spéciale que M. Magendie place dans les corps striés est une force purement

imaginaire." He found that these structures were quite inexcitable. "Chez les animaux vivants les corps striés semblent être complètement insensibles aux irritants mécaniques: ils peuvent être dilacérés sans qu'il y ait manifestation d'aucun signe de douleur, sans que la moindre contraction musculaire survienne. Les fonctions spéciales des corps striés restent encore à démontrer."

Meanwhile Julius Budge [11] (1840) was obtaining still other results by the somewhat crude methods we have been considering. "I opened the skull of a young dog who had just been killed, and in a few minutes completely exposed the whole brain. At the same time my assistant had opened the abdominal cavity and laid out the intestines. I cut away the cerebral hemispheres, raised up the corpus callosum, and irritated with a sharp needle the optic thalami, corpora quadrigemina, and corpora striata, one after the other. The stimulating of the corpora striata and quadrigemina increased the motions of the intestines every time. When the peristaltic motion had completely ceased, I could reproduce it by again stimulating these organs. . . . This continued to be the case for scarcely five minutes, and then the irritability was entirely destroyed." "Thus it is proved that the nervous principle of the motion of the intestinal canal is seated in the brain: nay, the spot is accurately determined from which it proceeds, or rather, in which the nerves of the canal are concentrated. The central organ of the motion of the stomach was also shown in my experiments: it is in the right corpus striatum."

Magendie's views received some support from subsequent investigators, among whom may be mentioned Schiff [69], Beaunis [4], Fournié [28], Lussana and Lemoigne [47], and Nothnagel [59]. Fournié made injections of chloride of zinc into the caudate nucleus (dogs), obtained strong progression movements, and concluded that in the corpus striatum were excitable centres sending nerve-impulses peripheralwards for the carrying out of voluntary movements. Beaunis employed injections of caustic soda, liquor ferri sesquichlorati, and ammonia carmine, and also obtained forced movements (rabbits), but the crudity of these experimental methods is sufficiently obvious.

Nothnagel employed a fine needle, or rather syringe, wherewith to inject minute quantities of pure chromic acid into the caudate. At a particular spot in that ganglion, dignified by him with the name of the "nodus cursorius," stimulation of this sort always produced violent forward movements in the rabbits on which he experimented. If we read the original description, however, we note that it was only after

an interval of from *two to ten minutes* that the animal "schliesslich in ein wildes Umherstürzen zum Teil mit Manègebewegungen und öfteren Anprallen an Wande, u.s.w., überging." The localizing value of the results is clearly infinitesimal. By stimulation of the lenticular nucleus after a similar fashion, especially in its anterior and middle parts, he obtained bending of the trunk with the concavity to the side of the lesion. He therefore endeavoured to distinguish between the caudate and the lenticular nuclei, placing in the former a centre for combined movements conditioned by psychical stimuli, and in the latter a centre for individual movements.

It might be supposed that the era of inexact experimentation would have passed whenever the method of electrical stimulation came into vogue. Such, however, at first, was far from being the case. In 1870 Hitzig [37] stimulated the lenticular nucleus by a special instrument ("Lanzenrheophor") through the frontal fissure, and obtained powerful contractions of the contralateral muscles, but the possibility of simultaneous cortico-spinal stimulation cannot be negatived. In 1874 Burdon Sanderson [68] adopted the simple expedient of dropping a needle vertically from the surface of the cortex and found it reached the corpus striatum in its posterior part at a depth of some 10 or 12 mm. Obtaining movements by stimulation at this point (cats), he concluded as follows: "From these facts it appears that the superficial convolutions do not contain organs which are essential to the production of the combinations of muscular movements now in question. They further make it probable that the doctrines hitherto accepted by physiologists, that the centres for such movements are to be found in the masses of grey matter which are to be found in the floor and outer wall of each lateral ventricle, are true."

It was in 1876 that Ferrier [23] published his well-known book, "The Functions of the Brain," which contains much of interest for our subject, and enables us to appreciate the way in which the corpus striatum was at that time generally regarded. One or two quotations may be given.

"The results of (electrical) stimulation of the corpora striata in monkeys, cats, dogs, jackals and rabbits are so uniform as to admit of being generalized together.

"Irritation of the corpus striatum causes general muscular contraction on the opposite side of the body. The head and body are strongly flexed to the opposite side, so that the head and tail become approximated, the facial muscles being in a state of tonic contraction, and

the limbs maintained in a flexed condition. Apparently the individual movements excited from the various regions of the hemisphere are all thrown into action simultaneously, the flexors predominating over the extensor muscles."

The same author, it may be remarked, makes the express statement that "individual or differentiated movements are not capable of being excited by application of the electrodes directly to the corpus striatum." The general conclusion come to is that "in the corpus striatum there would thus appear to be an integration of the various centres which are differentiated in the cortex." The same view is expressed again in other sections of the book. Thus: "The motor combinations which are integrated in the corpus striatum are again differentiated in the cerebral hemispheres."

Now, up to this epoch clinicians generally had been fully convinced that the corpus striatum was a motor organ, and differentiation between disease of that ganglion and disease of the pyramidal paths was not attempted. In fact the anatomical conceptions holding sway at that time were all for regarding the corpus striatum as an actual station on the path between cortex and cord. In 1866, for instance, Broadbent [10] said that "to the motor nuclei of the cord fibres descend in the antero-lateral white columns from the corpus striatum, decussating at the point of the medulla." It is hardly necessary to point out that this view assumes that the pyramidal paths issue directly from the corpus striatum. The same assumption is tacitly made in all the writings of the period, and occurs again and again in records of hemiplegic and other cases.

Although apparently attached to this opinion, Ferrier endeavoured to separate the function of the cortex from that of the basal ganglia. He states that "the various physiological and pathological data which have been advanced to show that destruction of the corpus striatum causes paralysis of voluntary motion . . . do not suffice to determine the special function of these ganglia as distinct from the cortical centres." He puts the problem very clearly when he says that "we . . . have to ascertain whether any special differences are observable between the symptoms resulting from lesions of the cortical centres and those following lesions of the basal ganglia, which may indicate what special functions these ganglia, as such, subserve."

After pointing out how greatly animals differ in respect to the degree of independent organization of motor activities in centres below the cortex (to which important consideration attention will subsequently be

devoted), the same experimenter concludes from the facts of comparative physiology that the corpora striata are centres in which habitual or automatic movements become organized. With the proviso that in man even the most habitual or most automatic actions require the co-operation of the centres of conscious activity, he holds that by virtue of a short circuit from afferent to efferent side, from the optic thalami to the corpora striata, movements in response to immediate sensory impressions take place, and that there is every reason to believe the basal ganglia suffice to a large extent for the execution of habitual movements.

These early views of Ferrier were based upon the assumption to which reference has already been made, that the peduncular or cortico-spinal fibres and the ganglionic substance of the corpus striatum formed a complex whole. The corpora striata were held by him to be the ganglia of interruption of the projection system of the foot or basis of the crus, "an anatomical indication of their motor signification." The integral connexion of the pyramidal path and the corpus striatum he regarded as established, and in view of our present-day knowledge it is historically interesting to note that at that date there was greater diversity of opinion in regard to the significance of the optic thalamus, the facts of pathology as far as the corpus striatum was concerned being supposed to be constant and uniform.

The theory that the actions which are regarded as inherited instincts, all the compound reflex, automatic, habitual actions of man, which had, through long-continued repetition, assumed the character of acquired instincts, were co-ordinated or integrated in the basal ganglia, seemed for a long time to satisfy the neurologist. It is odd to note, however, how carefully the writers of that time avoid declaring that automatic movements are actually *localized* in the corpus striatum. Ross [66], for instance, says that "all complex movements which animals manifest in response to emotional disturbances are *organized* in the corpus striatum." Speaking of a cat "spitting," he remarks: "The regulation of the movements concerned is *organized* in the corpus striatum, but the incitement to the action of these centres comes from the cortex." (Italics my own.) It is a little difficult clearly to follow this distinction, and Ross himself elsewhere hinted he had begun to doubt the subordination of the corpus striatum to the cortical motor centres. In fact, he says in another place: "The corpus striatum must be regarded as a nerve centre co-ordinate with, and not subordinate to, the cortex."

François-Franck and Pitres [29] (1878) exposed the corpus striatum in dogs by removing the cortex. They obtained no movements from

localized electrical stimulation of the caudate and lenticular nuclei: whenever the electrodes were applied to the internal capsule, there was a marked response. They found a striking contrast between the results of feeble stimuli applied to the internal capsule and strong stimuli applied to the corpus striatum. They considered the corpus striatum definitely inexcitable.

Already, however, Flechsig [24], and later Wernicke [79], and Charcot [14], were coming to the conclusion that the great majority of the fibres of the pyramidal system are uninterrupted on their way from cortex to crus through the basal ganglia and that the corpus striatum is a ganglion independent of the cortex, possessing no cortical projection - system. Whenever it was demonstrated that hemiplegia and hemianæsthesia were caused by injury to the fibres between the basal ganglia and not by lesions of the ganglia themselves, the importance of the corpus striatum forthwith diminished and once again its nature and functions became shrouded in obscurity. For a long time no work was done on the subject. Attention was directed rather to a study of the functions of the cortico-spinal system. Cases began to accumulate where lesions of the corpus striatum were unaccompanied by recognizable symptoms during life. The view was expressed that lesions of the lenticular nucleus, for instance, were always silent.

Since that time, opinion has been divided on the motor function of the corpus striatum. Its excitability has been as much denied as accepted. Luciani and Tamburini [46] considered that under given pathological conditions the caudate nucleus could take on the functions of the motor cortex (dogs, apes, rabbits). Lo Monaco and Bellanova [44] destroyed the nucleus caudatus in dogs, but, obtaining results more or less similar to those from lesions of the cortex, regarded the corpus striatum as an included portion of the motor cortex, and considered it closely connected with the latter. Bianchi [7] stimulated the corpus striatum with platinum needle electrodes in dogs and rabbits, and, obtaining in certain cases pleurosthotonus with movements of the head and extremities, held to the opinion of Hitzig, that the corpus striatum was electrically excitable.

Baginsky and Lehmann [3] (1886) considered the nucleus caudatus an integral part of the motor region of the brain (rabbits, cats).

From his experimental investigations Munk [58] (1884) came to the conclusion that the structure in question was concerned with habitual movements.

Johansen [39] (1885), experimenting on dogs, obtained tonic cramps

from stimulation of the lenticular nucleus, and concluded that that organ was concerned with the genesis of convulsions. In fact, he held that epileptiform seizures in man, unaccompanied with loss of consciousness, arose in the lenticular nucleus.

But other investigators, among whom may be mentioned Gliky [32] and Braun [8], obtained entirely negative results.

In 1889 [54] Minor performed a series of carefully planned experiments on rabbits, dogs, cats, and guinea-pigs. He showed clearly that the movements apparently elicited from stimulation of the caudate were due to overflow of the current to the neighbouring capsule. He repeated Nothnagel's experiments and demonstrated that the results came from the capsule, and in order to establish this beyond cavil he performed the crucial experiment of previously causing the whole pyramidal system to degenerate by removing the motor cortex. Thereafter he failed, even with strong currents, to obtain movements from the corpus striatum. The motor function of that organ, therefore, became more than ever doubtful.

In 1890, Ziehen [83] reached a similar conclusion (rabbits). He showed that not a few of the movements hitherto supposed to come from stimulation of the caudate in reality came from the genu of the capsule. He noticed that the nearer the stimulating needles were to the capsule, the more certain were the motor phenomena that resulted. When electrodes were pushed into the mass of the corpus striatum tonic convulsions followed after some thirty seconds, a condition which, in his opinion, could only be regarded as a capsular effect. With removal of the whole motor region, faradic stimulation of the lenticular nucleus was always negative.

Prus [65] (1899) in his experiments pushed the sinus longitudinalis aside, cut through the corpus callosum, and opened the lateral ventricles, exposing the ventricular surface of the caudate. He obtained tonic cramps in the contralateral limbs from stimulation of the posterior part of the caudate, clonic cramps from the middle, and running movements from the anterior section. In addition, he noted inhibition of respiration from stimulation of the middle division of the caudate, with elevation of blood-pressure and slowing of the pulse-rate. He concluded that some of his results were the expression of reflexes aroused by stimulation of afferent or sensory nerves, but that the tonic and clonic twitchings, and the rise of blood-pressure, were the direct result of electrical irritation. Prus supposed that the caudate played a part in voluntary movement and in automatic movements, such as running

or walking, and that it contained a vasomotor and vasoconstrictor centre.

Wieting [81] (1891) and Wertheimer and Lepage [80] (1897) found the corpus striatum inexcitable (dogs).

Probst (1901) destroyed the nucleus caudatus, leaving the capsule intact, and could not obtain any paralytic or even paretic phenomena.

In 1902, Schüller [70] repeated and revised these experimental methods, and once more the result was negative (dogs). The caudate, and corpus striatum generally, he always found inexcitable from an electrical standpoint. Schüller also observed quickening of respiration from stimulation of the caudate, especially in its anterior part, but no respiratory effect could be elicited when the capsule was allowed to degenerate. As, however, the acceleration of respiratory rhythm was more readily obtained from the caudate than from the capsule, he concluded that, possibly, there was a local connexion between the former and the capsular fibres concerned with respiration, which, in his view, were probably part of the cortico-thalamic system, passing to the median nucleus of the thalamus.

Stieda [73] (1903), after preliminary degeneration of the whole cortico-spinal system, directly stimulated the caudate in dogs, but obtained no movements whatever.

At various times during the last twenty years, v. Bechterew [6], in collaboration with one or other of his pupils, has performed experiments on the corpus striatum which have been collected and published in the second volume of " Die Funktionen der Nervencentra " (1909).

Von Bechterew's first series of experiments (dogs) were undertaken in 1886. After previously effecting complete degeneration of the pyramidal tract by extirpation of the motor area he was unable to obtain any motor phenomenon by strong stimulation of the caudate nucleus. Again, with Stieda, in 1902, similar researches were undertaken, but in every instance the result was negative. Von Bechterew concludes that it must be considered beyond dispute that the caudate nucleus has nothing to do with automatic movements, still less with volitional movements.

On the other hand, however, he reached a somewhat different conclusion with regard to the lenticular nucleus. With Schaikewitsch, in 1902, he experimented on dogs, either removing the hemisphere so as to stimulate the lenticular nucleus directly, or previously destroying the pyramidal system and then pushing an electrode for a given depth into the nucleus through the sylvian fissure. In the majority of his experi-

ments he obtained tonic contractions of the opposite limbs, and of the head and tail, and also generalized epileptiform convulsions on both sides of the body. He obtained these phenomena even when the pyramidal path was degenerated by preliminary extirpation of the motor cortex. Von Bechterew concludes that the lenticular nucleus has a motor function: that in the globus pallidus is a special tract of extra-pyramidal fibres stimulation of which effects movements on the opposite side of the body. The putamen he associates with the caudate nucleus, presumably denying to it any function of a like nature.

Grünstein [35] (1911) made lesions in the caudate and lenticular nuclei in dogs and rabbits with a specially constructed needle, but as his paper contains no mention of physiological results, and is concerned solely with the anatomy of the corpus striatum, it need not be further alluded to at present; due reference will be made to his anatomical findings in subsequent chapters.

In the review of the experimental literature on the corpus striatum that has been given, reference has been made more than once to a possible association of these masses of grey matter with the functions of the viscera, and some evidence has accumulated which goes to show that there may be connexions between the corpus striatum and the functions of respiration, circulation, and the maintenance of body temperature, as well as possibly the function of the bladder and alimentary tract. As my own experimental researches have been concerned with the motor part of the subject, this question may be left to one side for the present.

## Chapter II.—Personal Experimental Researches.

The research was carried out in the laboratory of experimental neurology at University College, under the ægis of Sir Victor Horsley, who performed my operations for me, and to whom I am very greatly indebted for much generous help and advice.

### *Methods.*

Some twenty-five monkeys were experimented on (*Macacus rhesus*, *Macacus sinicus*). Both stimulation and electrolytic methods were utilized. The instrument employed was the stereotaxic instrument of Clarke and Horsley [38], which is fully described in Brain, vol. xxxi, p. 45. It may be said here, very briefly, that its purpose is to direct a

needle in any one of three planes. The average size of rhesus heads varying very slightly within certain limits, a brass cage is devised, inside which the animal's head is fixed. The vertico-transverse plane which passes through the external auditory meatus on either side, known as the interaural plane, is taken as zero. On the brain of the rhesus it passes almost constantly just behind the upper limit of the fissure of Rolando. A horizontal plane passing through the inferior margin of the bony orbits and the external auditory meatus, known as the basal plane, is taken as zero for up and down measurements. By means of a series of photographs of vertico-transverse sections of a frozen rhesus head with the brain in situ, cut 2 mm. thick and numbered from the interaural plane forwards, it has been possible to decide with the greatest accuracy at what point to stimulate, or to electrolyze. Thus: a plane about 12 mm. in front of the interaural plane cuts through the three segments of the lenticular nucleus. The needle carrier is accordingly moved the requisite distance along a measured antero-posterior brass bar, which brings the point of the needle opposite this desired plane. Then the depth from the surface of the spot to be stimulated is measured on the photograph corresponding to the plane (to all the photographs a millimetre scale is appended) and found to be, say, 16 mm. The needle-point is therefore moved inwards 16 mm. from the surface of the cortex along the needle carrier, and we know for a certainty, if the carrier is at the correct height above the basal plane, that the point of the needle is somewhere in the globus pallidus. The precision of the instrument is admirable, and results were obtained from the very first.

The needle consists of a fine-drawn double capillary glass tube, inside which, insulated by the glass, are two fine platinum wires. At the end of the needle they are naked for the extent of less than half a millimetre, and when the other ends are connected up to a battery and a constant current allowed to flow, a limited electrolytic lesion is readily produced. In the series of experiments most of the lesions were made with a current of 3 to 5 ma. running for 5 to 15 minutes. The damage made by the passage of the needle through the cerebral tissues is astonishingly slight, and easily distinguishable afterwards from the main lesion.

It does not take long before one learns where the projection of the corpus striatum on the lateral aspect of the cerebral hemisphere is to be traced. If the point of the needle be introduced through the operculum, through the lower extremity of the third frontal gyrus, through the

upper or middle part of the superior temporal gyrus, it is certain to strike the lenticular nucleus at a depth of 12 to 16 mm. on vertico-transverse planes some 9 to 13 mm. in front of the interaural plane, which, as already mentioned, passes just behind the upper limit of the fissure of Rolando.

*Stimulation Experiments.*

In the great majority of the macaque monkeys experimented on it was made a routine practice to stimulate the lenticular nucleus electrically before proceeding to make electrolytic lesions. The procedure was as follows: The animals were always under deep anæsthesia induced by chloroform and continued with ether. By the help of the photographs of the normal macaque head, already referred to, it was a simple matter to determine the position of the point of the stimulating needle. A plane 10 mm. in front of the interaural zero plane was commonly chosen to commence with. In the vertical direction a plane about 12 or 13 mm. above zero usually brought the needle opposite the lower part of the gyrus overhanging the sylvian fissure; 10 mm. above zero was opposite the upper part of the superior temporal gyrus; 5 or 6 mm. above zero was opposite the middle part of the same gyrus. In this plane 10 mm. in front of the interaural zero, and on the 10 mm. plane above the base line, it was very commonly found that when the needle was driven into the brain for a distance of 10 mm. its point was on or just internal to the external capsule. By working forwards and backwards from the 10 mm. frontal plane, 2 mm. at a time, by carrying the needle upwards and downwards in each plane, and by advancing the needle-point 2 mm. at a time from the external capsule inwards to the internal capsule, it has been possible to stimulate systematically the whole of the lenticular nucleus in all its segments. Further, at any given point, it was made a frequent practice to commence with the secondary of a Kronecker coil at 500 on the scale, or even less, and to advance it to 1,000, 2,000, 5,000 or even 10,000 on occasion, without altering the needle position: in this way the results of current spread were easy of detection. A double needle was nearly always the one employed; in this way bipolar excitation was applied to very small areas. The current utilized was the faradic, derived from the coil above mentioned. Every gradation from feeble currents upward was readily and conveniently obtainable.

From what has been said it will be understood that the control over the position of the needle-point is complete, and that the operator is able to say at any given moment exactly what part of the lenticular

nucleus is being stimulated. So far from desiring to exclude pyramidal or cortico-spinal paths by previous section and subsequent degeneration, it was rather an advantage to have their integrity unimpaired, as the contrast between stimulation of the nucleus and of the capsular fibres was rendered so striking thereby as by itself to constitute satisfactory proof of the difference in electrical excitability between the two.

It may be said at once that the lenticular nucleus was found to be electrically inexcitable. In the first place, with the needle in the centre of the putamen, even comparatively strong currents failed to produce any discoverable motor phenomenon in any muscular group. This was noted again and again. The same is true also of the globus pallidus. An identical current, employed by way of control, was found to produce movements at once from the motor cortex. Whenever the immediate neighbourhood of the internal capsule was reached typical movements were obtainable, and with the needle in the capsule, of course, often powerful movements were elicited. It was frequently observed that with weak currents, advancing the needle-point merely 2 mm. made all the difference between no movement and a capsular movement, showing the genuine inexcitability of all but the corticospinal fibres. It may be definitely stated, as a result of the researches here described, that investigation of the whole of the lenticular nucleus with a stimulating needle has failed to elicit any evidence in the ape of the localization of motor centres there, comparable to the centres of the excitable motor cortex.

In the second place it occasionally happened that certain movements occurred while the nucleus was being explored with the needle, but these were always variable, inconstant, and fleeting. First of all it was sometimes found that homolateral movements of the face, mouth, or tongue took place from stimulation towards the outer surface of the putamen and the external capsule. These were neither strong nor persistent, and in any case they were far from constant. The mechanism of their production is interesting, but is outside the purpose of the present communication. Next, it was occasionally noted that blinking movements of both eyes occurred; the animal sometimes opened its eyes and stared straight in front, sometimes one or other or both eyes blinked; very occasionally the eyes rolled indefinitely and then came into a fixed midway position; sometimes the mouth opened slightly and symmetrically. It was impossible to obtain these movements with any regularity; oftener than not they were conspicuous by their absence. It cannot be

said that the occurrence of such movements, obtained for that matter in the stimulation of quite other areas and dependent to some extent on the degree of anæsthesia, is any indication of their being localized in the nucleus lentiformis. My experiments have uniformly failed to demonstrate the occurrence of tonic contractions of the opposite limbs, and epileptiform convulsions, such as v. Bechterew [6] says he obtained from stimulation of the lenticular nucleus. The fact must not be lost sight of that the animals he experimented on were dogs, whereas my experiments were on monkeys.

Again, it was observed occasionally that a particular movement, say slight closure of the contralateral hand, was produced by stimulation with the needle-point close to the capsule, judged by its distance in from the surface, and that stimulation with the needle advanced a further 2 mm. produced the same movement much more powerfully and unmistakeably; under such circumstances there can be no doubt that in the first instance the movement was not truly lenticular in origin but resulted merely from the propinquity of the needle-point to capsular fibres and from spread of current.

Thus from a consideration of the above-mentioned data it is clear that when due precautions are taken, when exact control both of current and of position of needle is possible and is practised, stimulation of the lenticular nucleus, both putamen and globus pallidus, is essentially negative. In this respect my research but confirms the work of those previous investigators who have performed their experiments in a sufficiently careful and accurate fashion.

### *Electrolytic Lesions.*

(1) *Physiological results.*—It has already been stated that for the production of electrolytic lesions a constant current of from three to five or more milliampères was utilized, and allowed to run for some five to fifteen minutes. Both small and large lesions were made, the latter by making two, three, or four smaller lesions close together. While in some instances the lesions were intentionally placed, for anatomical reasons, in the vicinity of, but outside the nucleus lentiformis, reference will now be made solely to those in which they were situated entirely within the nucleus.

The animals were allowed to live as a rule for some three weeks after the operation. In practically every instance uninterrupted recovery took place. During these weeks the animals were tested in

all sorts of ways: they were allowed to climb about the room used as a monkey-house, they were tried with the use they made of objects in either hand, their reflexes were examined, &c.

For reasons which will be mentioned subsequently, in the first monkeys experimented on the lesions were single and small. None of these animals showed any sign of motor impairment that careful and repeated examination could detect. No involuntary movements, *e.g.*, of the nature of tremor, were noticed. In the later series of experiments, where the lesions were larger, involving the greater part of the nucleus, the absence of any involuntary movement was again noted. Some of these monkeys, however, showed a preference, in the taking of nuts or bananas, for the homolateral limb. Or, in climbing about their cage, they showed just the least awkwardness or clumsiness with the contralateral limbs. Yet no approximation to paralysis or even paresis was seen. It was impossible to satisfy oneself that there was any undeniable alteration in the tone of the muscles of the limbs opposite to the lesion. In several instances the tendon reflexes were slightly increased in the contralateral limbs. There was no defect of sensibility as far as could be ascertained.

In one or two cases it is possible that slight implication of some capsular fibres may account for the motor symptoms, such as they are; in others, however, microscopical examination failed to demonstrate capsular degeneration, and yet the animal's limbs on the side opposite to the lesion were not perfectly normal. It is therefore conceivable that a large lenticular lesion produces an unsteadying effect in innervation. But the data at my disposal preclude any elaboration of this. All that can be said is that small and large lesions alike failed to reveal themselves by any obvious or constant or unequivocal defect of motility, as far as the results of the present investigation are concerned. In this series, as a matter of fact, no bilateral lesions were made.

The opportunity was taken, in a number of cases, of stimulating the homolateral motor cortex after large lesions in the lenticular nucleus. The result in every instance was the same; no difference in excitability could be detected between corresponding points on the right and left motor cortical areas. These excitation experiments were made after the full three weeks, *i.e.*, after degeneration secondary to the lesion was thoroughly established. Thus there is no physiological evidence of impairment of function of the motor area from large lesions in the homolateral corpus striatum.

(*B*) *Anatomical results.*—As already stated, the animals operated on

under strict antiseptic precautions were allowed to live about three weeks; they were then killed under an anæsthetic. The brain was at once injected in situ with formol-Müller, removed, and the position of the interaural plane marked on it. A few days later it was cut in 2 mm. slabs, parallel to the interaural plane, by means of Clarke's macrotome. The slabs showing the lesions were then photographed, and the material duly prepared for examination by Marchi's method.

In the following pages a selection only from the complete set of investigations will be given. It will be understood that a description of each would result in much overlapping, and also that in some animals the results were scantier or less instructive than in others.

The preliminary remark may be made that at first the electrolytic lesions were intentionally very small. In the case of such complicated fibre areas as the globus pallidus it is essential that the lesions should be small, and in this respect the immense superiority of the accurate technique obtainable by the stereotaxic instrument is especially seen. No method other than that which it has been my privilege to utilize can be of equal service. By tracing minute degenerations first of all it is possible to unravel the degenerations of larger lesions much more readily.

I. Rhesus 248 09.—The lesion is quite small, and placed in the anterior dorsal portion of the right putamen (fig. 1).

The area of the putamen involved in the lesion is almost exactly one-quarter of its vertical height, and one-half of its breadth. The lesion extends back from the anterior limit of the putamen to where the lateral zone of the globus pallidus begins, i.e., it involves about one-fourth of the putamen considered antero-posteriorly, as seen on horizontal section.

*Degenerations.*

(1) There is slight degeneration from the needle track ventrally in the external capsule.

(2) The slight degeneration from the needle track of scattered cortical fibres, mostly in the white matter underlying the gyri of the island of Reil, need not be further specified.

(3) From the site of the lesion in the putamen there is very well marked and easily followed fine degeneration in numerous bundles or pencils of fibres, all, without exception, degenerating in a ventral, caudal, and mesial direction, towards the mesial plane. The degeneration is strictly confined to fibre bundles on the mesial side of the lesion, i.e., there is no degeneration in a dorsal or lateral direction. The degenerated bundles gradually converge as they pass caudally and ventrally, and fresh bundles of normal fibres appear in their place. When the lamina medullaris lateralis is reached the affected bundles have converged towards the junction of its dorsal and middle thirds. Extremely few

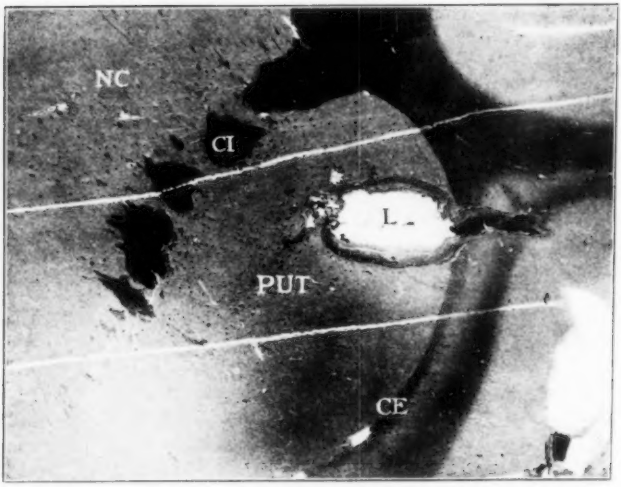


FIG. 1.—Rh. 248/09. Lesion in the anterior and dorsal portion of the putamen.

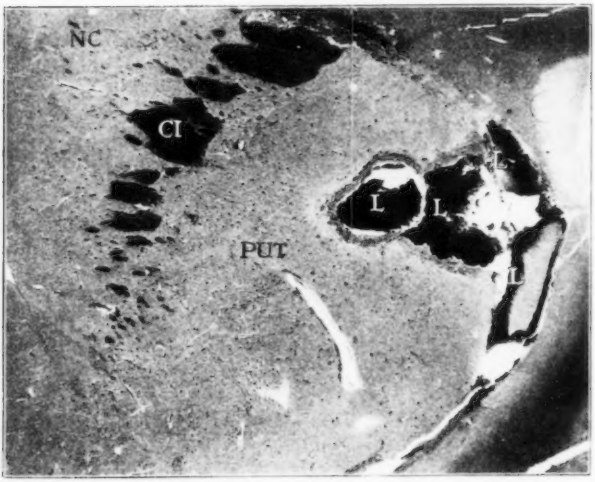


FIG. 2.—Rh. 280/09. Large lesion in putamen, which has spread round its margin.

degenerated fibres are to be seen leaving the bundles to enter the lamina; by far the greater number of them pass directly across. In the middle zone—lateral division of the globus pallidus—the affected bundles have converged still more, but the degeneration does not become diffused. The fibres keep closely together, and can be traced mesially as a narrowing pencil, gradually losing its degeneration, across the middle zone, across the lamina medullaris medialis, to end by diffusing out in the centre of the mesial division of the globus pallidus. By this time complete new bundles have taken their place in the putamen and lateral zone of the globus pallidus. None of the degenerated fibres crossing the mesial lamina pass either dorsally or ventrally in it. As the degenerated pencils travel caudally and ventrally, they gradually diminish in quantity, particularly after reaching the middle zone.

(4) None of the degenerated fibres reach the optic thalamus. None of the degenerated putamen fibres enter the internal capsule. There is no degeneration in the ansa lenticularis.

II. Rhesus 280·09.—The lesion is large, and as it were double. It occupies the whole of the lateral portion of the putamen and extends mesially half way across the nucleus, destroying vertically at least a third of it. It is mainly the anterior portion of the putamen that is involved in the lesion. In addition the bubbles of gas have made their way anteriorly and dorsally, round the external capsule, separating it from the putamen and destroying the margin of the latter. The lesion has cut across a considerable number of cortical fibres entering the internal capsule on the anterior side (fig. 2).

*Degenerations.*

(1) The degeneration in the external capsule passes ventrally but soon disappears, however, and is not so much as might be expected considering the position and degree of the lesion.

(2) There is marked degeneration of cortical fibres from the dorsal aspect of the lesion, many passing outwards to the cortex and others turning across the corpus callosum.

(3) There is abundant degeneration of fine fibres in the putamen, in bundles all passing mesially and at the same time ventrally and caudally. The amount of degeneration from the lesion in the putamen is exactly proportional to the size of the lesion, as is also the case in Rb. 248, showing that the degeneration originates in the putamen. The degenerated bundles occupy at least one-third of the vertical height of the nucleus, and can be traced easily across the lateral medullary lamina, across the lateral zone of the globus pallidus and the mesial lamina, to the centre of the mesial zone of the globus pallidus. As they traverse the nucleus they converge but keep in bundles even where the fibres are closely amassed together, gradually diminish in quantity of degenerated fibres, and diffuse out well across the mesial zone. They give off a few degenerated fibres to the lateral lamina—only a small proportion of the total—and only one or two to the mesial lamina. They cannot be traced beyond the globus pallidus. They do not enter the ansa lenticularis.

(4) There is a slight degeneration from the putamen across the upper third of the internal capsule into the caudate; numbers of healthy fibres come in the reverse direction.

(5) There is marked coarse degeneration of a large number of capsular fibres, readily traceable because of its striking contrast to the fine degeneration of putamen fibres. As they run side by side the two types can be easily distinguished (fig. 3). The degenerated capsular fibres do not give off any to enter either of the laminæ medullares. A few which pass from the capsule at these points are found on serial section to be aberrant bundles which converge on the main body of degenerated fibres a little further ventrally. No degenerated fibres enter the globus pallidus from the capsule.

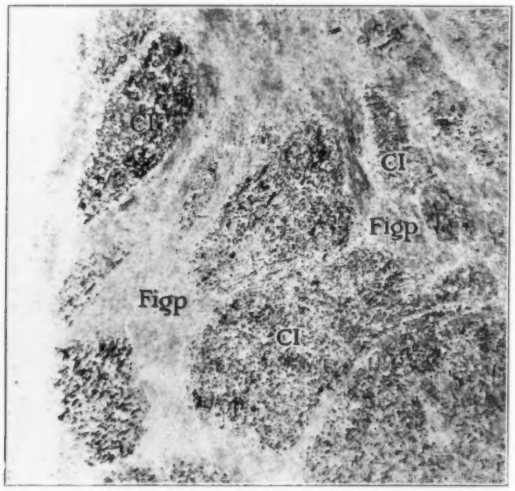


FIG. 3.—Rh. 280/09. Contrast between coarse capsular degeneration and fine internuncial fibre degeneration (scarcely visible with this magnification).

III. Rhesus 292/09.—The lesion is intentionally small, and almost identical with that of Rh. 248.

*Degenerations.*

(1) The usual putamen degeneration is present. All degenerated fibres pass in a caudal, ventral, and mesial direction; none degenerate in a dorsal, oral, or lateral direction. The degenerated pencils of fibres can be traced to the mesial zone of the globus pallidus; they give off very few fibres to pass into either of the laminæ. There is no degeneration into the optic thalamus or caudate, or of the ansa. The amount of degeneration from the putamen lesion is proportional to its size.

(2) One or two fine bundles of degenerated fibres are seen apparently entering the putamen from the external capsule in its dorsal and anterior section. The presumption is that these have degenerated from the needle track, for they are well beyond the degenerated putamen area and they may be of putaminal origin and have coursed on the surface of the putamen. They skirt the internal capsule and apparently enter it. At the most there are about three such bundles, and they are very small.

IV. Bonnet 316/09.—The lesion is further back in the putamen, and is of interest because of its propinquity to the lateral medullary lamina (fig. 4).

*Degenerations.*

As the lesion is rather small the degenerated putamen bundles of internuncial fibres cannot be traced so far, but they are at their maximum

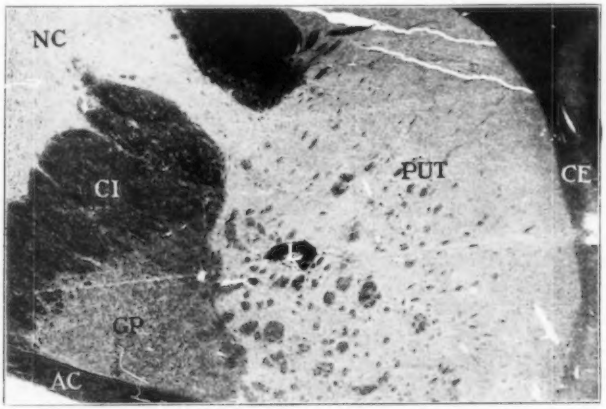


FIG. 4.—Bonnet 316/09. Small lesion in putamen, near the lateral medullary lamina.

when they cross the lateral medullary lamina, whence it is easy to determine that in this instance no fibres of these bundles leave the latter to pass dorsally or ventrally in the lamina. Healthy laminal fibres can be seen passing through some of the degenerated pencils.

V. Rhesus 348/10.—The lesion is in the corona radiata just dorsal to the anterior extremity of the internal capsule; it has in no way implicated the putamen, while it has caught a large number of capsular fibres from the operculum and lower motor area.

*Degenerations.*

(1) There is gross capsular degeneration, not, of course, complete. The degenerated fibres are coarse and easily followed. No degenerated capsular fibres enter either the lateral or the mesial medullary lamina. No degenerated

fibres enter either the lateral or the mesial zones of the globus pallidus. None enter the putamen.

(2) There is marked degeneration of associational cortical fibres in various directions.

(3) A very slight descending degeneration occurs in the external capsule.

(4) Incidentally, it is seen that a considerable degeneration of fibres in the corpus callosum is present; most make their way to the opposite cortex, but a fair number turn and enter the opposite internal capsule.

(5) A few degenerated fibres "cut the corner" of the putamen to enter the internal capsule.

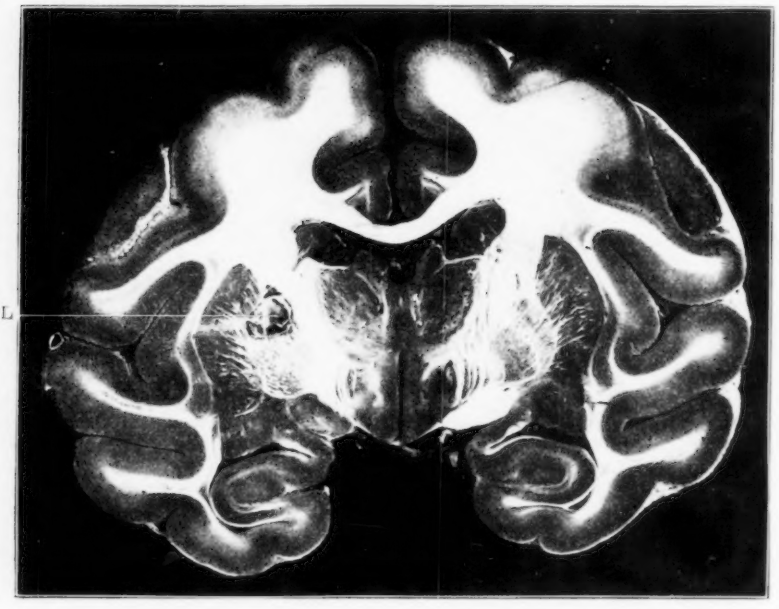


FIG. 5.—Rh. 434/10. The lesion is mainly in the lateral division of the globus pallidus.

The results of such an experiment as this go far to show that the fibre-content of the putamen is autogenous in origin.

VI. Rhesus 434/10.—The lesion occupies the dorsal anterior portion of the lateral zone of the globus pallidus in its whole transverse extent, as well as the adjacent mesial portion of the putamen and the lateral portion of the mesial zone of the globus pallidus. It has completely destroyed the dorsal half of the lateral medullary lamina, and impinges very slightly on the internal capsule about the junction of its dorsal and middle thirds (fig. 5).

*Degenerations.*

(1) There is slight but definite degeneration of some lenticulo-caudate fibres from the lateral zone of the globus pallidus across the internal capsule. A much greater number of healthy fibres come in the opposite direction.

(2) A fine degeneration passes ventrally in the crescentic lateral lamina, but only in small quantity does it reach the base of the lamina. Caudal to the lesion new healthy fibres soon appear in the lamina. A large number of fine fibres entering the nucleus by the lamina are degenerated; they do not follow the lamina in its whole extent, but leave it to pass into the putamen and the lateral zone of the globus pallidus: they are internuncial fibres from the caudate.

(3) There is considerable degeneration of fine bundles crossing the middle lenticular zone radially, below and behind the level of the lesion, and running mesially into the mesial zone; some of these gradually edge towards the capsule and cross it obliquely, reaching the level of the mesial zone before they start to cross; they can be followed into the lateral and ventral sections of the optic thalamus (strio-thalamic fibres). The granulation in these fibres, though fine, is perhaps not quite so fine as in the pure putamen degenerations.

It is noteworthy that considering the extent of the lesion none of the involved fibres seem to travel far; they are all short; the longest are the strio-thalamic. A number of the radial degenerated bundles, towards the centre of the nucleus, do not pass the mesial zone; after reaching well across it they diffuse out.

(4) In addition to the radial degeneration there is well-marked degeneration of transverse fibres in the middle lenticular zone, i.e., fibres more or less parallel to the course of the lateral medullary lamina. Their calibre is somewhat coarser, and their degeneration is more scattered or diffused; they can be traced ventrally and posteriorly to the ventral part of the middle zone, where most of them are brought together, and then turn again in a mesial direction as the ansa lenticularis. The degeneration of these tranverse fibres is just as marked as the degeneration of the radial fibres.

(5) Most of the radial fibres crossing the internal capsule obliquely are seen to be making their way to the corpus subthalamicum. It is clear that none of these radial fibres blend with the internal capsule in its basal third.

VII. Rhesus 450/10.—The lesion is analogous to that in Rh. 434, but it has invaded the internal capsule somewhat (fig. 6).

*Degenerations.*

(1) The main degenerations are identical with those obtained in the preceding animal. There is marked degeneration of strio-thalamic fibres, which can be followed mesially far into the thalamus as little bundles of degenerated fibres, keeping closely together until they diffuse out.

(2) The radial and transverse degenerations are as before. More degenerated fibres enter the ansa. The degeneration in the lateral lamina soon ceases.

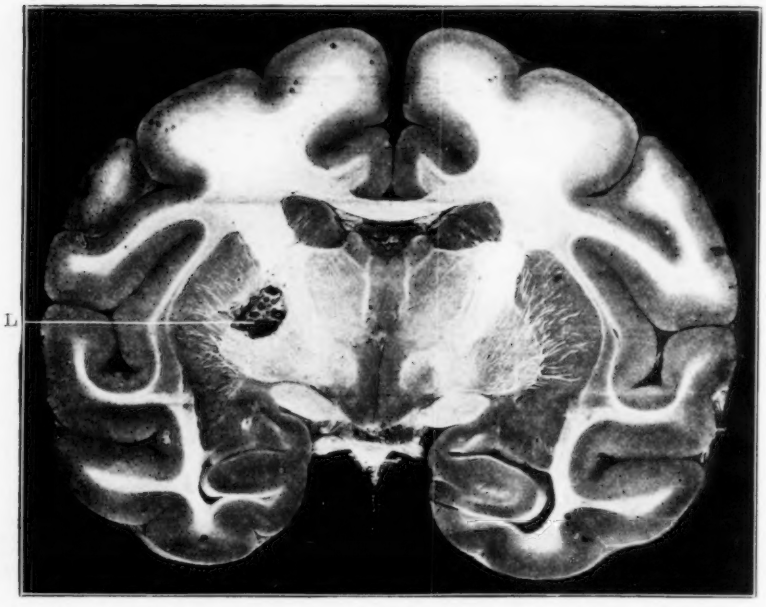


FIG. 6.—Rh. 450/10. The lesion is mainly in the lateral division of the globus pallidus.

FIG. 7.—Rh. 488/10. The lesion is situated outside the putamen, at its posterior ventral extremity.

(3) Most of the degenerated radial bundles edging towards the capsule run obliquely into the corpus subthalamicum; others belonging apparently to this group can be traced in a mesial, caudal and ventral direction beyond the corpus subthalamicum apparently to the lateral part of the capsule of the red nucleus.

(4) There is well marked degeneration of the transverse fibres (part of the ansa lenticularis) in their anterior division, i.e., that part which turns round the extremity of the capsule to reach the anterior ventral corner of the optic thalamus (the *Hirnschenkelschlinge* of older writers).

VIII. Rhesus 488/10.—This experiment was made to determine whether any fibres enter the putamen from behind and below. The needle has passed through the superior temporal gyrus and the lesion is situated in the claustrum and external capsule at the posterior ventral extremity of the putamen, which itself is not touched by the lesion (fig. 7).

*Degenerations.*

(1) No degenerated fibres enter the putamen from its lateral side: all skirt the nucleus without entering, except a few cortico-spinal or cortico-pontine fibres which "cut the corner" of the putamen, but can very easily be shown to be merely fibres of passage.

(2) There is well marked degeneration in a dorsal direction in the external capsule, much more than in the other animals where the degeneration travelled ventrally.

(3) Various degenerations of cortical associational fibres need not be further specified.

IX. Rhesus 502/10.—The lesion is in the ventral portion of the lateral zone of the globus pallidus, destroying the ventral third of the lateral lamina and impinging on the mesial lamina. It has partially invaded the substantia innominata (figs. 8 and 9).

*Degenerations.*

(1) There is well marked ascending degeneration in the external capsule and in the fibres of the insula. It is interesting to note that a number of degenerated fibres enter the corpus callosum, but none at all pass into the putamen.

(2) The most caudal part of the lesion, the exact situation of which is seen in fig. 10, is excellently placed to show that some cortico-pontine fibres pass across the putamen in its caudal section merely as fibres of passage; there is no trace of any degeneration of putamen pencils. The degenerated fibres of passage are coarse and not fine.

(3) The double (transverse and radial) degeneration from the globus pallidus already referred to is particularly well seen. The transverse fibres, constituting an integral portion of the ansa lenticularis, are grossly degenerated, and readily traceable across the internal capsule somewhat obliquely to Forel's field and beyond. The radial fibres, in fine coalescing bundles, cross the capsule much more obliquely to end in the corpus subthalamicum; some of these are also found passing ventrally to the latter, skirting its ventral margin

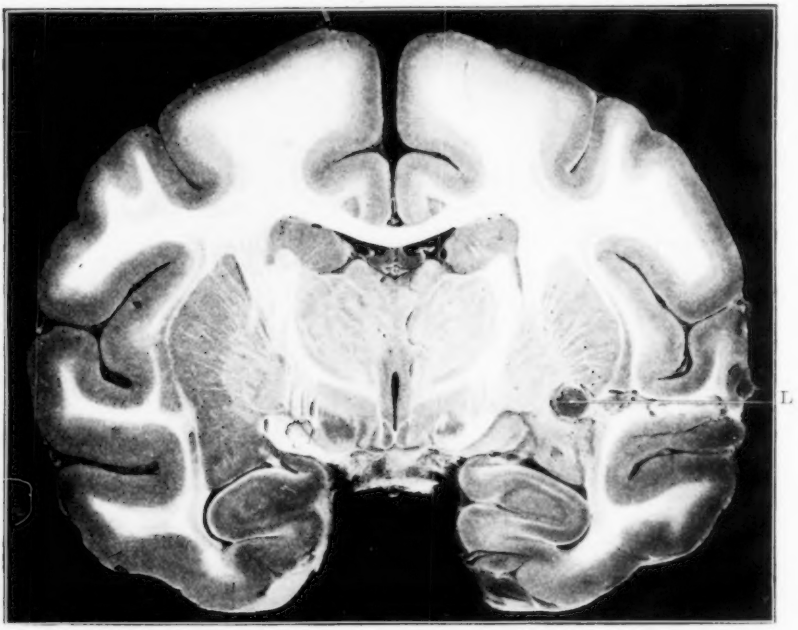


FIG. 8.—Rh. 502/10. The lesion is ventral in the putamen and globus pallidus.

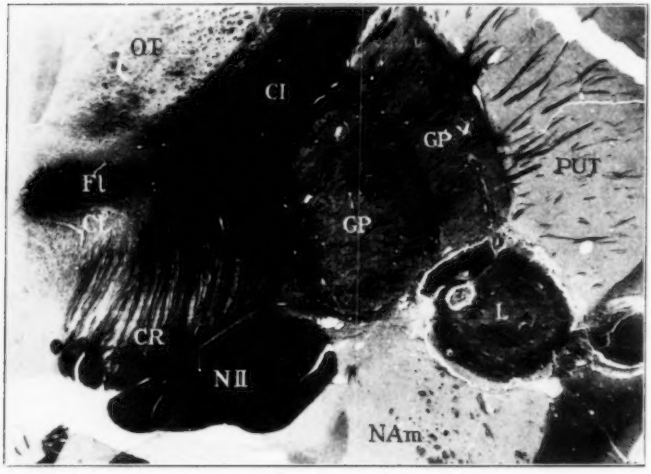


FIG. 9.—Rh. 502 10. Photograph of stained section to show exact position of part of the lesion.

FIG. 10.—Rh. 502/10. The most caudal portion of the lesion is well placed to decide whether cortico-striate fibres enter the nucleus from below or behind.

FIG. 11.—Rh. 26/11. Large lesion destroying putamen.

to end in the substantia nigra. Both of these degenerations are very complete, and owing to the integrity of the capsule they are easy to follow. The former is clearly visible travelling in a caudal and ventral direction as far as the ventral capsule of the nucleus ruber. The fibres going to the substantia nigra come from the most ventral of the ansa group. They pass mesially in a more or less horizontal fashion, and correspond to the tractus strio-peduncularis of Edinger.

(4) There is well marked but quickly disappearing dorsal degeneration in the lateral medullary lamina.

(5) There is no trace of any degeneration passing laterally in the nucleus

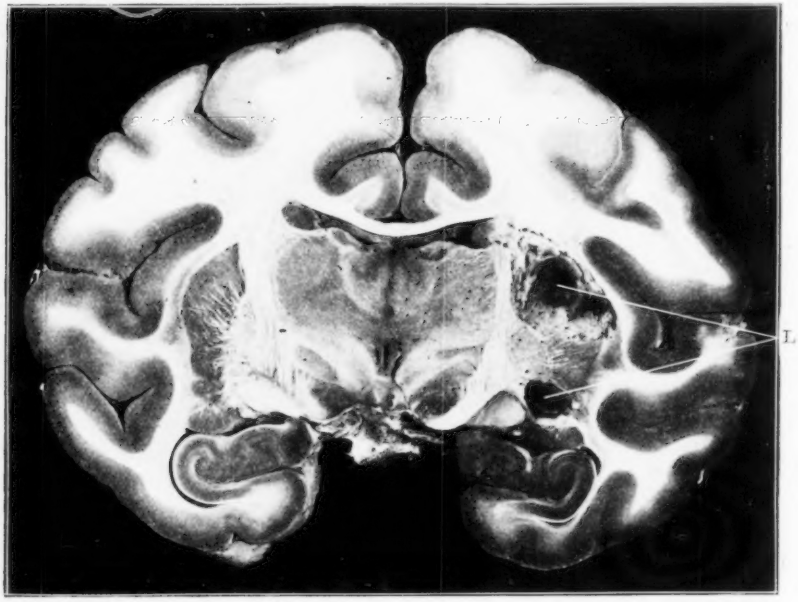


FIG. 12. Rh .26.11. The inferior lesion is placed ventrally in the putamen and globus pallidus

or along the laminæ, i.e., no indication of thalamo-cortical fibres passing by the laminæ or otherwise through the nucleus to the cortex.

X. Rhesus 26/11.—The main lesion, a large one, has destroyed the whole of the putamen and part of the lateral zone of the globus pallidus. The external capsule is completely destroyed about its middle (fig. 11). The posterior portion of the lesion has invaded the capsule and spread across it to the caudate. A second lesion, independent of the above, is placed in almost identically the same position as the lesion of Rh. 502, and from it important degenerations can readily be followed (fig. 12).

*Degenerations.*

(1) The external capsule is degenerated dorsally and ventrally, but no fibres leave it to enter the putamen, in front of, or behind the main lesion, except one or two small bundles which cross to join the internal capsule. A solitary degenerated fasciculus was seen apparently entering the putamen from the external capsule and so remaining.

(2) Certain cortical associational fibres that are degenerated need not be further specified.

(3) There is well marked, fine degeneration in the region between the caudate and the optic thalamus—the stratum subcaudatum of Sachs.

(4) There is considerable degeneration of strio-thalamic fibres passing mainly into the nucleus lateralis, but also, in less degree, beyond it.

(5) The typical degenerations of the ansa lenticularis across the capsule to Forel's field and beyond, to the capsule of the nucleus ruber, are obtained, as well as the radial degeneration of fine bundles more obliquely across the capsule to the corpus subthalamicum (strio-luysian fibres), and to the substantia nigra.

(6) There is no unequivocal evidence of degeneration spreading laterally in the putamen from the ventrally placed subsidiary lesion above noted.

(7) Some degenerations of cortico-thalamic fibres need not be further specified.

XI. Rhesus 96/11.—The lesion is a double one: the chief part is in the middle of the putamen and the lateral zone of the globus pallidus; an extension from this has spread dorsally across the internal capsule; the second lesion, from which important degenerations can be traced, is situated in the ventral part of the globus pallidus, close to, but entirely independent of the neighbouring internal capsule (fig. 13).

*Degenerations.*

(1) In the globus pallidus both radial and transverse degenerations are pronounced, and readily distinguishable. The former consists of a fine degeneration of converging pencils of fibres: some are merely internuncial fibres, passing from the lateral to the mesial zone of the globus pallidus: others, the majority, can be followed into and through the capsular fibres, which are easily separable owing to their relatively large calibre, to the regio subthalamica. Most pass to the corpus subthalamicum: some travel further mesially, either through or round that body, to diffuse out just in front of the area where the tractus cerebello-tegmentalis passes into the nucleus ruber. It is difficult to say whether they effect any definite union with the nucleus ruber. A number of fine degenerated fibres, belonging to this group, are also traceable into the substantia nigra.

The second or transverse degeneration of rather thicker, medium-sized fibres, which at first are less compactly arranged, consist of two parts, an anterior and a posterior. The latter, constituting the major part of the degenerated fibres, can be followed with ease more directly across the internal capsule as Forel's lenticular bundle ($H_2$) into Forel's field (fig. 14). Here the

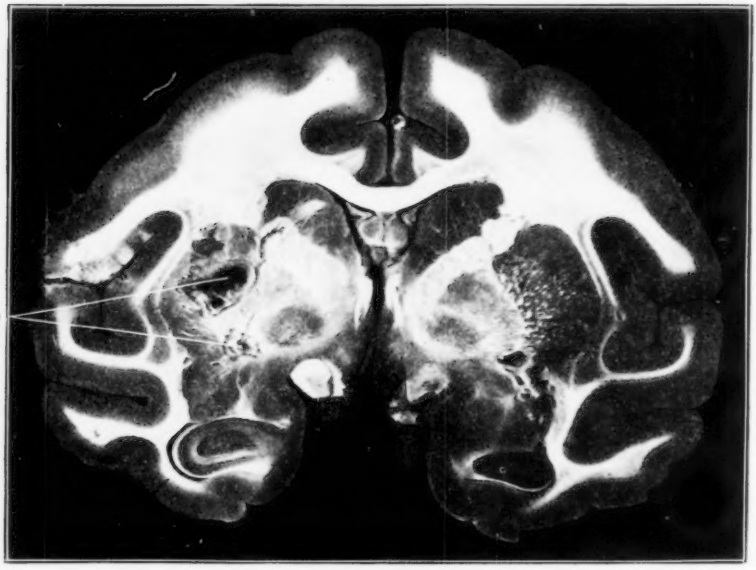


FIG. 13. – Rh. 96/11. Double lesion, both dorsal and ventral in the nucleus lentiformis.

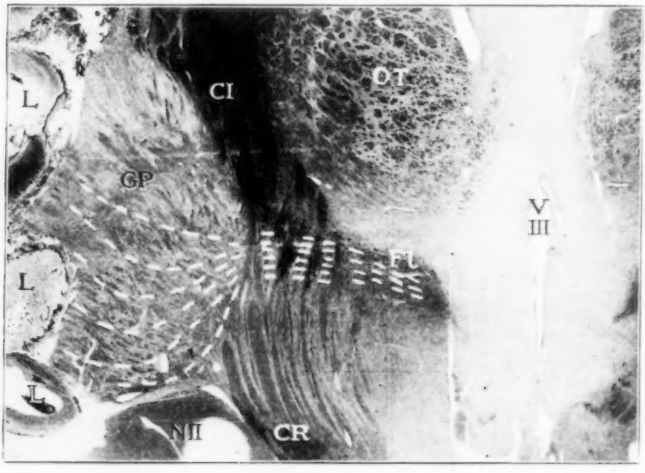


FIG. 14.—Rh. 96 11. The dotted white lines indicate the course of the transverse ansa lenticularis from the globus pallidus to Forel's field—the dorsal capsule of the corpus subthalamicum.

fibres have converged more and the degeneration is consequently intense (fig. 15). This tract of fibres passes mesially across the field and partially subdivides. The more dorsal fibres appear to end in a sort of rounded "nucleus" near the middle line (though from this "nucleus" some fibres pass ventrally to join the others), while the more ventral portion, somewhat larger, passes ventrally, caudally and mesially, and is definitely traceable to the lateral and ventral capsule of the nucleus ruber, where the degeneration ends. The anterior portion of the transverse degeneration, less in amount than the posterior, is seen to course round the ventral end of the internal capsule, passing between its fibres only in part, to reach the most anterior lateral and ventral corner of the optic thalamus. Of this anterior group, not

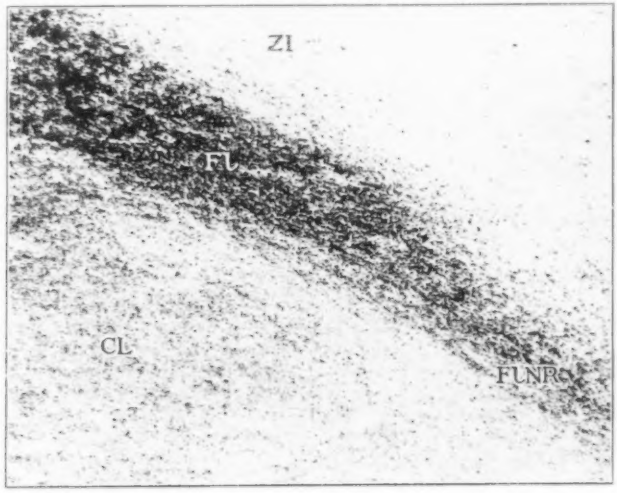


FIG. 15.—Rh. 96/11. Intense degeneration of Forel's lenticular bundle from a lesion of the globus pallidus. A portion of it passes to the capsule of the nucleus ruber.

a few, nevertheless, once they have crossed to the thalamus, turn ventrally and can be traced eventually to join the main posterior group in Forel's field.

(2) Strio-thalamic fibres are severely degenerated. They cross the capsule more or less at right angles, and diffuse out mainly in the nucleus lateralis, but some travel further, in small bundles, mesially across the thalamus to the neighbourhood of the median nucleus.

(3) The stratum subcaudatum of Sachs contains many fine degenerated fibres.

(4) Anterior to the main lesion, degeneration is traceable in both medullary laminæ. This passes dorsally in each instance, and can be seen to reach across

the upper third of the capsule to the nucleus caudatus, more particularly in the case of the mesial lamina in this instance.

(5) There is a well-marked fine degeneration along the dorsal aspect of the anterior commissure.

(6) A certain number of cortico-thalamic fibres are degenerated from the upper capsular lesion and are traceable into the ventral section of the thalamus. Across the mesial part of the zona incerta a few degenerated fibres are seen which have passed ventrally through the thalamus.

XII. Rhesus 116/11.—The main lesion is placed in the ventral part of the lenticular nucleus, extending over two-thirds of the nucleus in an antero-

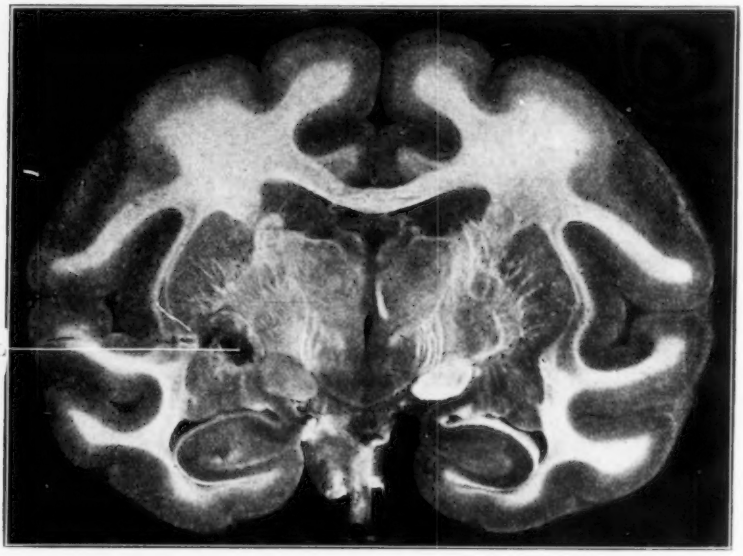


FIG. 16.—Rh. 116/11. The lesion is ventral in the lenticular nucleus.

posterior direction. It has passed beyond the strict limits of the nucleus ventrally, invading the dorsal portion of the nucleus amygdalæ external to the optic tract, in the area of the substantia innominata sublenticularis of Reichert (fig. 16).

*Degenerations.*

(1) There is considerable degeneration of lenticulo-caudate internuncial fibres, of fine calibre, passing from the putamen round the capsule to the caudate nucleus. Similarly there is much degeneration of fine internuncial fibres in both medullary laminæ. Some in the lateral lamina pass across the

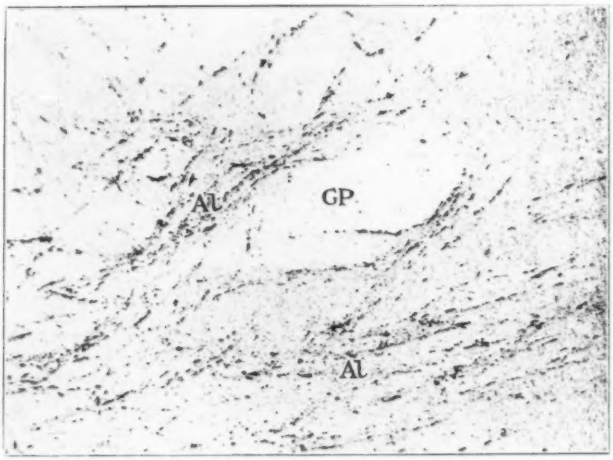


FIG. 17.—Rh. 116/11. Degeneration of the transverse ansa fibres in the globus pallidus, before they leave it.

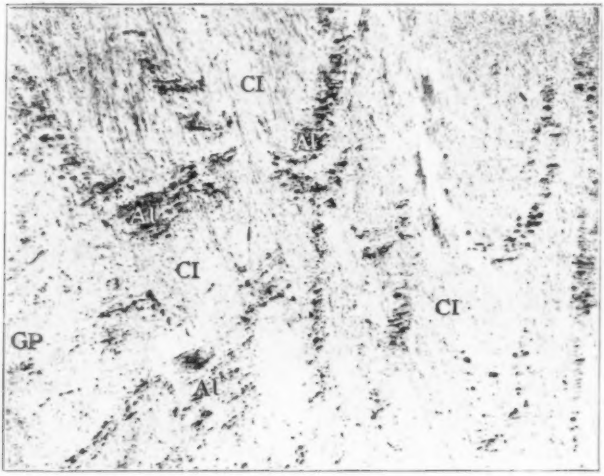


FIG. 18.—Rh. 116/11. Degenerated fasciculi of the ansa curving across the intact internal capsule.

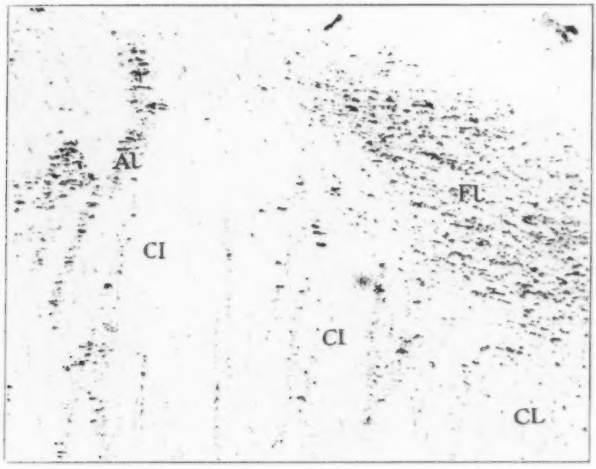


FIG. 19.—Rh. 116/11. Degenerated ansa fasciculi reaching Forel's field after curving across the intact internal capsule.

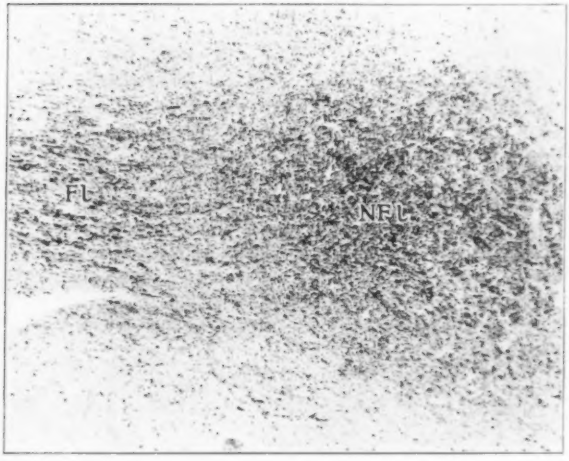


FIG. 20.—Rh. 116/11. The so-called nucleus of Forel's field, when the fibres take a different course, many passing ventrally and mesially to the capsule of the nucleus ruber.

capsule to the caudate, others turn off the lamina to enter the globus pallidus. The degenerated fibres pass dorsally in each instance.

(2) Fibres of fine calibre also pass across the capsule from the globus pallidus to the caudate in small quantity but quite definitely. These are from the lateral part of the lateral zone of the globus pallidus only.

(3) There is gross degeneration of the ansa lenticularis, and its fibres, medium in size, are very well seen as they converge towards the internal capsule, crossing it in more or less parallel curving fasciculi to enter Forel's field (figs. 17, 18, 19), across which they course mesially, partially subdividing into two groups: some end in a rounded "nucleus" at the mesial extremity of Forel's field (fig. 20), while the majority pass caudally, ventrally and mesially in a somewhat diffuse bundle and end by merging in the lateral and ventral

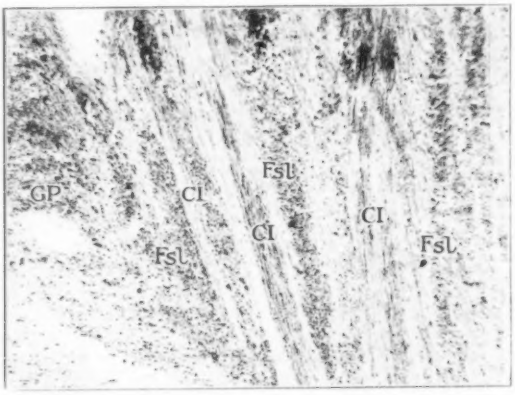


FIG. 21.—Rh. 116/11. The radial ansa fibres passing obliquely across the basal third of the capsule to the corpus subthalamicum.

capsule of the nucleus ruber. The anterior section of the ansa lenticularis, as described in Rh. 96, can be seen turning round the ventral extremity of the capsule to reach the antero-lateral and ventral margin of the optic thalamus. Again, some of its fibres then turn definitely in a ventral direction and join the main group in Forel's field.

(4) The radial lenticulo-fugal fibres, fine in calibre, constituting another part of the ansa lenticularis, are also grossly degenerated. They are readily traceable partly as strio-luysian fibres passing to the corpus subthalamicum (fig. 21); many, however, pass mesially to diffuse out in the area between the body of Luys and the nucleus ruber; a few pass into the substantia nigra. It is difficult to determine whether any of either part of the ansa cross the middle line; a few appear to cross in the commissure of Forel to reach the opposite nucleus ruber.

(5) There is marked degeneration of fine fibres along the dorsal aspect of the anterior commissure.

(6) There is a notable degeneration of Meynert's commissure as it lies just posterior to the optic tract. The degeneration is in an anterior and mesial direction from the lesion.

(7) There is no evidence of lateral degeneration from the lesion, in any fibres of the putamen (fig. 22).

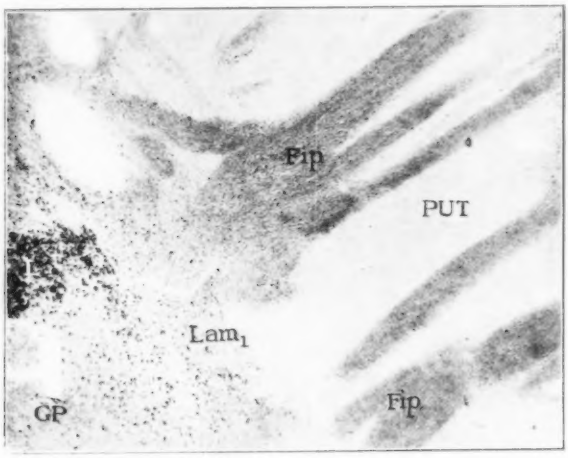


FIG. 22.—Rh. 116 11. Absence of lateral degeneration from lesion in nucleus.

## CHAPTER III.—ANALYSIS OF ANATOMICAL RESULTS OF PERSONAL RESEARCHES.

A study of the small and strictly localized lesions produced according to the technique employed for the purposes of this investigation, shows that in several important respects experimental data serve to confirm and elaborate certain views as to the anatomical relations of the corpus striatum hitherto not received with any approximation to unanimity.

The fibre system of the corpus striatum may be divided into four main groups:—

(1) Fibres arising and ending within the corpus striatum (internuncial).

(2) Fibres arising in the corpus striatum and ending elsewhere (striofugal).

(3) Fibres arising elsewhere and ending in the corpus striatum (striopetal).

(4) Fibres passing through the corpus striatum, but arising and ending elsewhere (fibres of passage).

I. In the first group several subdivisions may be distinguished.

(*a*) *Internuncial fibres from the putamen to the globus pallidus.*—These are invariably of fine calibre, with a delicate myelinated sheath. They are massed into bundles or pencils, arising by the approximation of individual fibres, not always very close to their cells of origin, and running mesially; the anterior pencils converge as they pass in a posterior direction, while the posterior converge as they travel anteriorly; the most ventral run in a dorsal direction, the dorsal in a ventral direction, and in this fashion they all converge towards the lateral zone of the globus pallidus; here some of them diffuse out, while others pass on to the mesial zone, where they in turn diffuse out.

(*b*) *From lateral to mesial zone of the globus pallidus.*—Similarly fine myelinated fibres arise in the lateral zone of the globus pallidus and cross mesially in radial bundles to the mesial zone.

(*c*) *From caudate to putamen.*—Many fine internuncial fibres pass across the dorsal third of the internal capsule from the nucleus caudatus to the putamen, while others reach the lateral zone of the globus pallidus.

It is perhaps worthy of note that distinctly fewer fibres pass from the putamen to the caudate than in the reverse direction; and this is true also of the connexions between the globus pallidus and the caudate.

*The composition of the laminæ medullares.*—In the present series of experiments lesions have been placed both at the dorsal and the ventral extremities of the laminæ medullares. In one or two instances a degeneration has been obtained extending from end to end of the lamina; as a rule, however, the degeneration takes place along a limited length, the affected fibres then turning either into the putamen or the globus pallidus. Even the longest degeneration obtained is essentially of a finely granular type, indicating the small calibre of the laminal fibres—an important consideration. The lateral lamina is composed in great part of caudate associational fibres passing in both directions. Some of the putamen-globus pallidus fibres enter into its constitution for a short distance. The mesial lamina, similarly, is composed of short connecting fibres passing both dorsally and ventrally; these are mainly internuncial fibres between the lateral and mesial zone of the globus pallidus for a part only of their course; from a lesion in its ventral

extremity the dorsally passing degeneration does not, as a rule, extend to the capsule. Caudate associational fibres are also found in it. Its ventral section blends with and is reinforced by a number of transverse, slightly thicker, fibres, termed by Dejerine [17] supplementary medullary laminæ, which go to form part of the ansa lenticularis, to be subsequently described.

It is always easy to distinguish between the fine degeneration of the short intermuncial fibres and the coarse degeneration of cortico-spinal fibres; the difference is unmistakeable. Laminal fibres running close to or passing through the capsule can readily be separated from the latter. The experimental evidence here furnished, therefore, negatives the view of Obersteiner [60] and others, who place in the laminæ thalamo-cortical fibres in part of their course, and that for two reasons. Firstly, as has just been remarked, the laminal degeneration is always one of fine-calibred myelinated fibres; and, secondly, in this series of experiments, no fibres have been seen passing corticalwards along the laminæ and so out of the nucleus. In fact, no indication of degeneration passing laterally, ventrally or dorsally out of the globus pallidus or putamen (except at their extremities) from lesions in various parts of these nuclei has been obtained. The conclusion is important, and reference will be made to it again immediately. Dejerine [17] states that from lesions of cortico-pontine, cortico-thalamic, and cortico-bulbar projection-fibres in man there is pathological evidence that fibres, not of lenticular origin, pass from the cortex by the lamina medullaris medialis to the corpus subthalamicum. I have obtained no experimental proof of the existence of these fibres in apes.

II. In the second group there are also important subdivisions.

(*a*) *Strio-thalamic fibres.*—These constitute the minor portion of striofugal fibres to the optic thalamus and regio subthalamica. They are derived from the mesial groups of radial bundles of the globus pallidus, and cross the internal capsule obliquely in its basal third to reach the lateral and ventral sections of the thalamus. They can be traced passing mesially across the thalamus and diffuse out in the neighbourhood of the internal nucleus; a fair number, however, do not extend beyond the nucleus lateralis. Although Dejerine [17] regards the strio-thalamic group as arising in part from the putamen and caudate, I have failed to trace any degeneration into the thalamus from lesions strictly confined to the putamen. Caudate-thalamic fibres perhaps exist in small quantity. Probst [62], however, could not find any after

lesion of the caudate, and my own experiments have failed to reveal certain evidence of their existence. Similarly, Grünstein [35] could find no trace, in rabbits and dogs, of caudate-thalamic fibres from lesions in the caudate. A group of fibres belonging to the ansa lenticularis, and corresponding to the *Hirnschenkelschlinge* of older writers, is, strictly speaking, part of the strio-thalamic system, since it passes from the globus pallidus to the optic thalamus. Reference will be made to this tract of fibres in the following description of the ansa lenticularis.

(*b*) *Strio-subthalamic fibres.*—The ansa lenticularis is a somewhat complex fibre system, in which, however, certain subdivisions are readily distinguishable.

(*a*) The chief set of fibres in the ansa stands out unmistakeably as composed of fibres slightly larger in calibre than the others, which are of the same size as the internuncial fibres already described. This tract arises in the lateral and mesial zones of the globus pallidus, runs more or less at right angles to the radially disposed pencils and is distinguished in the descriptions of experiments given above as the transverse group. It passes directly across the capsule in a slight curve with the convexity dorsal, and constitutes a closely set bundle reaching and occupying Forel's field. It corresponds to the lenticular bundle of Forel ($H_2$). The fibres pass mesially across Forel's field and form a sort of nucleus (*noyau du champ de Forel*—Cajal [13]) at a point where the general direction of the fibres changes slightly from a latero-mesial to a more antero-posterior direction. Many then pass ventrally and caudally and can be definitely traced to end in the ventro-lateral and ventral capsule of the nucleus ruber (figs. 23, 24). It seems possible, from one or two of my experiments, that a few fibres continue across the mesial plane by the decussation of Forel to reach the contralateral red nucleus.

This is the main group in the ansa lenticularis, and the definiteness of the anatomical connexion between the globus pallidus and the nucleus ruber is of considerable importance. It is easy to distinguish these fibres from those of the capsule, indeed from any other tract in the neighbourhood.

Von Monakow [56] states that the ansa is derived mainly from the putamen, but for apes this is certainly incorrect, as I have never found degeneration in the ansa from lesions confined strictly to the putamen. In a case examined by Tarasewitsch [75], the ansa was intact though there was a large lesion in the putamen. Grünstein [35] found a few degenerated fibres in the ansa from putamen lesions (dogs). Von Monakow [56] also

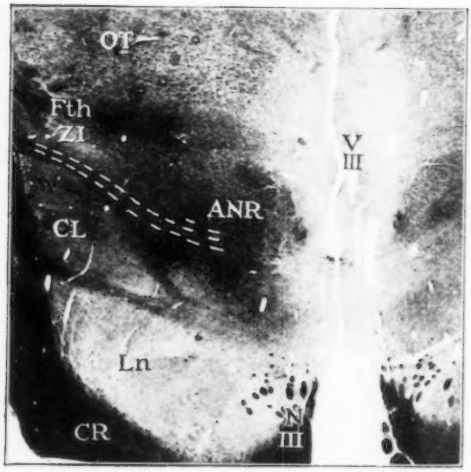


FIG. 23.—Rh. 116/11. The white dotted lines indicate direction taken by lenticulo-rubral fibres.

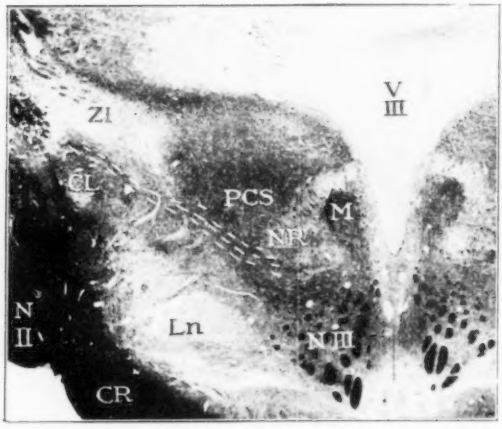


FIG. 24.—Rh. 116/11. The white dotted lines indicate the way in which fibres of ansa, from the globus pallidus, reach the capsule of the nucleus ruber.

states that some of the fibres in Forel's field edge dorsally across the zona incerta to reach the ventral portion of the optic thalamus, but I have not been able to satisfy myself of the existence of such fibres in apes. Sachs [67] was able to put a small lesion in Forel's field by the methods utilized in this series of experiments, and he found that from it a mesial degeneration passed caudally, ventrally and mesially to the ventral capsule of the nucleus ruber. Dejerine [17] admits the independence of the ansa and capsular fibres, and describes the former as reaching the capsule of the nucleus ruber in man. Edinger [21] mentions he has found negative evidence of the existence of the same connexions in the dog: after complete cortical extirpation some fibres running with the otherwise entirely degenerated cortico-rubral tracts remained; they were seen to be fibres passing from the corpus striatum to the capsule of the red nucleus. Flechsig [25] and v. Bechterew [5] had previously suspected the existence of this important relation. Cajal [13] states very positively that Forel's bundle and field consist of fibres of capsular origin. "Les auteurs considéraient ce cordon comme une dépendance du corps strié et un système tout à fait étranger au pédoncule cérébral. C'est le contraire qui est précisément la vérité. Il est tout simplement un groupe considérable de collatérales issues à angle droit du trajet des fibres motrices du pédoncule cérébral." He makes the absolute statement that no fibres of the lenticular bundle cross the capsule entirely. It is impossible, nevertheless, to subscribe to these views, which are completely refuted by my own and other experimental evidence. Cajal agrees that the fibres of Forel's field almost certainly reach the capsule of the red nucleus, and remarks that "nous ne cacherons pas que l'hypothèse d'une terminaison totale ou partielle du cordon de Forel dans le noyau rouge est loin de nous déplaire, car elle comble une lacune laissée par l'observation anatomique." Probst [64] also holds that the bundle in question is of lenticular origin, as did Forel [27] originally, followed by Mahaim [50] and v. Monakow [55]. It may be mentioned in passing that no degeneration has been found in Forel's field in amyotrophic lateral sclerosis. Both Probst and v. Monakow state that the lenticular bundle of Forel (the dorsal capsule of the corpus subthalamicum) passes mesially and ventrally to the tuber cinereum, forming a fasciculus tuberis cinerei. But I can find no proof of such connexions in these experiments on apes. Probst even states he has traced fibres across to the corpus geniculatum externum of the opposite side.

In v. Monakow's [57] recent monograph on "Der rote Kern, die

Haube, und die Regio subthalamica," no reference to the possibility of a connexion between the corpus striatum and the red nucleus is given, nor is it indicated in any of v. Monakow's diagrams—an omission (unless a reference has been overlooked) which is curious in view of the above mentioned investigations of previous observers and of the fact that there is a description of the nucleus ruber and its relations in the cat, dog, ape, &c., in the monograph.

Allusion has been made above to a more anterior portion of the ansa lenticularis composed of fibres of similar calibre, which edges round the mesial extremity of the internal capsule to reach the ventrolateral margin of the optic thalamus anteriorly. It constitutes the most anterior part of the transverse ansa fibres, and is of smaller dimensions than the other. While some of its constituent fibres do pass somewhat vertically in the thalamus, others turn ventrally once they have reached it and can be traced eventually to join the main caudal group in Forel's field.

(*β*) The second division of the ansa lenticularis is composed of slightly finer myelinated fibres arising from the radial bundles of the globus pallidus. They are ventral to the striofugal group to the nucleus ruber just described, and they edge across the basal third of the capsule much more obliquely. They can be traced across the capsular fasciculi as the latter extend into the crus. The great majority pass into the corpus subthalamicum (strio-luysian fibres) and diffuse out in its interior. Some, nevertheless, cross it completely and make their way to the neighbourhood of the lateral capsule of the red nucleus, approaching it from in front. It is difficult to determine whether they effect any union with the nucleus.

A smaller number of fine fibres pass obliquely across the crus in a mesial direction, ventral to the corpus subthalamicum, to reach the locus niger.

Edinger [21] describes fibres of capsular origin entering the body of Luys, but they have not been demonstrated in my series of experiments. Cajal [13], similarly, alludes to capsular fibres, derived solely from the ventral part of the cerebral peduncle, and entering the body of Luys, but elsewhere he says that it is possible they are really striofugal fibres. The ventral fibres proceeding from the mesial globus pallidus to the substantia nigra are less in number than might be supposed from the comparative prominence assigned them by Edinger, who gives them the name of tractus strio-peduncularis. No evidence of the occurrence of such fibres in man has as yet been advanced, according to Dejerine [17].

By way of résumé, the following account of the constitution of the ansa lenticularis as determined by experiments on apes may be given :—

It consists of two divisions, distinguishable by slight differences in the calibre of their constituent fibres. The first is made up of medium-sized fibres running transversely from the lateral and mesial globus pallidus across the internal capsule; its more anterior section reaches the lateral and ventral corner of the thalamus by rounding the ventral end of the capsule; its main posterior section forms Forel's lenticular bundle, crosses Forel's field, whence a good part of it extends ventrally and caudally to reach the ventral capsule of the red nucleus. The second is constituted by fine fibres from the radial bundles of the globus pallidus, which edge obliquely across the basal third of the capsule; the majority (mostly dorsal and middle bundles) end in the corpus subthalamicum, but some cross this mesially and turn caudally to end, apparently, in the immediate neighbourhood of the anterior capsule of the red nucleus; others (a few ventral bundles) pass ventrally to the corpus subthalamicum, and end in the substantia nigra.

No reference has hitherto been made to certain other parts of the regio subthalamica, viz., the zona incerta and the thalamic bundle of Forel ($H_1$), for the simple reason that in none of my numerous experiments on the globus pallidus has any degeneration been traced into either of these areas. On the other hand, when the internal capsule has been suitably injured, there has been an evident degeneration of cortico-thalamic fibres passing mesially and ventrally along, and forming a part of, the thalamic tract of Forel ($H_1$). At its caudal and mesial extremity some fibres make their way to the dorsal aspect of the nucleus of Forel's field. But no degeneration has been seen to pass to $H_1$ from the dorsal capsule of the body of Luys (Forel's lenticular bundle), as is mentioned by Dejerine[17] to be the case. No degeneration has been found from the globus pallidus to the zona incerta. Yet Edinger [21] declares that more or less all of the fibres crossing the zona incerta come from the ansa lenticularis, an opinion to which it is impossible to subscribe, as far at least as the ape is concerned.

(*c*) *Striofugal fibres to the internal capsule or cerebral peduncle.*—No unequivocal proof of the passage of fibres, fine or medium, from either the putamen or the globus pallidus to the internal capsule or crus has been obtained. The general direction of the two divisions of the ansa lenticularis is always oblique to that of the cortico-spinal fibres. Sir Victor Horsley has examined my specimens independently and agrees that they furnish no evidence of such a passage.

Probst [63] has failed to find any fibres with this course. Dejerine [17] concurs in admitting the independence of the ansa and the capsule. Prus [65] thinks there are centrifugal fibres from the putamen to the crus, but offers no anatomical evidence of these, which, for that matter, the work of other investigators and myself renders more than problematical.

(*d*) *Strio-cortical fibres.*—One of the noteworthy findings in this series of experiments has been the absence of any degeneration passing laterally from the lesions in the putamen and globus pallidus. In the putamen, for instance, no trace of outward degeneration from the lesions has been noted. From laminal lesions no degenerated fibres passing by the laminæ have been traced out of the corpus striatum to the cortex. Internuncial fibres may degenerate lateralwards from lesions of the globus pallidus, but they are easily recognizable as such. Without, therefore, enlarging on this matter further, it may be stated that strio-cortical fibres are non-existent.

Apart from thalamo-cortical fibres crossing the corpus striatum—to be referred to subsequently—Probst [63] found no association fibres between the nucleus lentiformis and the cortex after experimental lesions of the former, and my results corroborate his in this respect.

(*e*) *Connexions between the corpus striatum and contralateral structures.*—In a recent communication van Valkenburg [77], working on the corpus callosum, says: "More than one preparation led me to suppose that a part of the corpus callosum serves to connect the neostriata on each side, i.e., the nucleus caudatus and putamen. But I have not been able to find . . . . a convincing proof of this. In analogy with the archistriatal commissure which connects the nuclei amygdalæ, and a possible commissure between the palæostriata in Meynert's commissure, such a connexion of the phylogenetically most recent parts of the striatum would not be improbable." It has just been remarked, however, that there is no trace in apes of fibres passing out of the globus pallidus or putamen in a dorsal or lateral direction to the white matter of the hemispheres (van Valkenburg's experiments were on mice, rabbits, and cats). There is no evidence, *a fortiori*, of striofugal fibres reaching the corpus callosum, for the ape, at least.

In one only of my experiments was there indication of fibres crossing from Forel's field by the commissure of Forel to the contralateral red nucleus. They were very few in number. Sachs [67] has found such fibres degenerating from an electrolytic lesion in Forel's field. Dejerine [17], however, says they go "probably" to the contralateral body of

Luys; but the evidence I have to offer, such as it is, corroborates the description given by Sachs.

It has been held that the corpus subthalamicum is connected with the contralateral nucleus lentiformis by the intermediation of Meynert's commissure. This view has been supported by Darkschewitsch and Pribytkow [16], as well as by v. Bechterew [5]. Dejerine [17] says he has seen degeneration of the commissure of Meynert after lesions of the globus pallidus, with integrity of the optic bandelette. In more than one of my experiments an exquisite degeneration was traceable along Meynert's commissure from one side to the other. It is, however, quite clear from a careful scrutiny of the sections in a number of my experiments that Meynert's commissure has nothing to do with the globus pallidus. Only when the lesion has impinged on the margin of the optic bandelette has Meynert's commissure degenerated. Lesions in the globus pallidus, completely destroying its ventral part, and involving the ventral ansa lenticularis, have left Meynert's commissure intact. Where it has been degenerated the fibres cross neither to the corpus subthalamicum nor to the nucleus lentiformis. The view which places the origin of the fibres of Meynert's commissure in the corpus geniculatum internum is probably correct.

III. In the third group there are again a number of separate tracts.

(*a*) *Thalamo-striate fibres.*—As none of my own lesions were placed in the thalamus, it is not possible for me to confirm or deny, on experimental grounds, the existence of thalamo-striate fibres. It is known, however, that such do occur, the association between the thalamus and the caudate being close (Edinger, Dejerine, Sachs). Reference is made to these for the sake of completeness.

(*b*) *Subthalamo-striate fibres.*—From a lesion in Forel's field Sachs [67] has found degeneration passing laterally across the capsule in its basal third, and entering the globus pallidus, where it diffused out. No degenerated fibres entered the putamen. This degeneration resulted from the involvement of fibres passing in a reverse direction in the main part of the ansa lenticularis. Similarly, Dejerine (case Gardette) was able to follow degeneration from a lesion in the regio subthalamica: (1) mesially, according to the lines already fully described, and (2) laterally, by the ansa lenticularis and Forel's lenticular bundle to the globus pallidus. It would appear, therefore, that while the ansa lenticularis and the strio-subthalamic tracts are to a very large extent striofugal, they also contain striopetal fibres. Such fibres are, no doubt, to be

expected, for it is a general rule that cerebral areas of grey matter are united doubly, though not always equally, to each other, by afferent and efferent fibre-systems.

(c) *Cortico-striate fibres.*—The experiments herein detailed show sufficiently that the corpus striatum is independent of the cerebral cortex. A few small fasciculi may cross the dorsal, ventral, oral or caudal aspects of the putamen from the cortical side, but they are fibres of passage. With practically complete capsular degeneration no fibres have been seen to leave the cortico-spinal path and enter the lenticular nucleus by its

FIG. 25.—Rh. 80/11. (Not given in text.) The photograph indicates part of the comprehensive lesions made to demonstrate the independence of the lenticular nucleus. No cortico-striate fibres were found.

laminæ or otherwise (fig. 25). Occasionally aberrant bundles may leave the capsule to diverge towards the lenticular nucleus, but they invariably join it again. No sign of Cajal's collaterals from the cortico-spinal system which arborize among the cells of the lenticular nucleus, and, according to him, transmit voluntary motor excitation, has been discovered. Besides, the calibre of the cortico-spinal group is distinctly larger than that of the fibres of the corpus striatum.

The consensus of opinion among investigators is in favour of the independence of the corpus striatum and the cerebral cortex. A century ago Burdach [12] showed that the appearances suggested that the putamen was not connected with the cortex, and no evidence has been adduced to combat the contention; neither strio-cortical nor cortico-striate fibres exist. Marinesco [51] alone has maintained that as a result of complete or partial destruction of the frontal lobe (in apes and dogs), fine degenerated bundles of fibres can be traced into the corpus striatum, more particularly the caudate. Apart from the inexactness of such general experiments, Cajal [13] could not find any trace of such fibres and says there are no direct cortico-striate connexions. So also Dejerine and many others. The absence of any such anatomical paths renders nugatory Mingazzini's [53] hypothesis of subordinate motor centres in the lenticular nucleus under the influence of the cortex. All the anatomical and experimental evidence goes to demonstrate the complete autonomy of the corpus striatum.

(*d*) Cajal places in the lenticular nucleus and caudate *collaterals from the fillet*, ascending sensory fibres, whose exact origin he does not further specify. There is no experimental evidence for the existence of such fibres in apes. It is perhaps scarcely worth mentioning now that the view formerly held by Flechsig [25] and v. Bechterew [5] of a participation of fillet fibres in the ansa lenticularis is quite discredited since the researches of v. Monakow [55] and Mahaim [50].

IV. There remains the final question of any fibres of passage running for part of their course through the corpus striatum.

(*a*) *Thalamo-cortical.*—The experimental evidence in this matter has already been considered. It negatives the possibility of such fibres passing in part by the laminæ of the lenticular nucleus, and is thus definitely opposed to the views of Probst [63], Obersteiner [60], and others. Tschermak [76] believed that fillet fibres made a loop-shaped excursion through the nucleus lentiformis on their way to the cortex, but assent to this view cannot be accorded. In one instance only, it should be said, have I found fibres whose relative calibre proclaimed their extra-striate origin degenerating in a lateral direction from a lesion in the lateral zone of the globus pallidus. They were not laminal fibres. In all some two or three small fasciculi were seen to contain somewhat coarse Marchi granules, and they were traced lateralwards out of the putamen. In view of the fact that identical lesions in other animals failed to reveal any such fibres, those just mentioned must be considered aberrant bundles presumably of thalamo-cortical fibres.

In number they were quite insignificant, while the fact that they passed out of the putamen a little more centrally than the fasciculi previously alluded to, which "cut the corners" of that structure, is perhaps a sufficient reason for making a reference to them at all.

(*b*) *Cortico-thalamic.*—It has been held, similarly, that some of this group pass by the laminæ medullares of the lenticular nucleus, but there is no evidence of such a route in apes.

(*c*) *Cortico-luysian.*—Dejerine [17] says that "le corps de Luys . . . reçoit de la corticalité cérébrale quelques très rares fibres qui passent par les lames médullaires du globus pallidus." However this may be in man, I cannot find them in the apes on which experiments have been made.

## Chapter IV.—Physiological and General Considerations.

The problem of the function of the corpus striatum in man, difficult as it is, is brought nearer solution by a consideration of the anatomical (human and comparative) and clinico-pathological sides of the question, each of which will be found to furnish a material contribution to the subject.

(1) It is essential in discussing the physiology of the corpus striatum to think anatomically. Admitting the not infrequent error of supposing that anatomical juxtaposition argues physiological relationship, it is, nevertheless, a more serious mistake to assign functions to an organ which it is anatomically incapable of carrying out. Now we have seen that the cardinal anatomical connexions of the corpus striatum are as follows:—

(i) It is independent of the cerebral cortex.

(ii) The putamen and caudate are closely linked to each other, and both to the globus pallidus.

(iii) The main striofugal and striopetal fibre-groups are related to the globus pallidus only, and not to the putamen and caudate directly.

(iv) The striofugal groups preponderate, and link the globus pallidus with the optic thalamus and the regio subthalamica, including the nucleus ruber, corpus subthalamicum, and substantia nigra.

(v) The corpus striatum is not connected directly with the spinal cord.

(vi) The corpora striata are, directly at least, independent of each other.

From a consideration of these anatomical data, obtained by experi-

ments on apes, and known to be, in great part, if not entirely, identical in man, it is clear that the corpus striatum is an autonomous centre; in other words, whatever its function, that function is exercised independently of the cerebral cortex. Further, these anatomical data indicate that that function is motor in type, i.e., that it is exercised in an efferent or caudal direction. It does not, however, follow that because the main connexions are efferent the motor function of the organ is identical with, or even similar to, the motor function of the cortico-spinal system.[1]

Certain other anatomical features may here be referred to. By far the greatest number of the cells of the corpus striatum in man are small and of a more or less spindle or spherical and only slightly polygonal type, with scanty cytoplasm. It is mainly in the globus pallidus that larger cells are to be found; the former have short axons, the latter longer axons, and they belong to the striofugal group of neurons. There are not, however, in the corpus striatum large polygonal cells unmistakeably of the type of the Betz cells of the motor cortex or the ventral cornual cells of the spinal cord. Again, the calibre of the internuncial fibres is very fine, and that of the larger of the ansa fibres is less than that of the fibres of the adjacent cortico-spinal system. Without laying unjustifiable emphasis on these structural differences, they may, I think, be taken at least to suggest that the function of the corpus striatum and its projection-system is not, in man, identical with the function of the motor cortex and its projection-system.

For anatomical reasons, therefore, apart from any other considerations, the possibility of the existence in the corpus striatum of "centres" in any way analogous to those of the gyrus precentralis must be regarded as very doubtful. Brissaud [9], Halipré [36], and others, explained the phenomena of pseudobulbar paralysis by placing hypothetical centres for articulation in the corpus striatum, but Brissaud apparently imagined that the ansa lenticularis joined the cortico-bulbar and cortico-spinal systems. There is, however, no direct anatomical path to the

[1] An additional anatomical fact not without interest is that the globus pallidus and its projection-system, the ansa lenticularis, become myelinated comparatively early in fœtal life, but the significance of this fact is debateable. As the myelin appears first near the cells of origin and appears progressively towards the ends of the fibres, it may be taken to indicate the direction of the nerve impulses. It is usually held that the appearance of myelin coincides with the assumption of functional activity on the part of the fibre, but this view is not of universal applicability. Edinger [18] says it is surprising that the basal forebrain bundle does not always become myelinated early, *e.g.*, in the young frog and salamander, and holds that "if medullary sheaths are developed whenever certain portions of the brain come into active use, then there are highly organized animals which do not make use of their forebrain."

appropriate motor nuclei from the corpus striatum. No movements akin to the movements of articulation can be obtained by stimulation of the putamen or globus pallidus in apes,[1] and we shall see later that phylogenetic evidence indicates that in man it is unlikely that the corpus striatum should possess more elaborate motor functions than in apes. Mingazzini [53] imagines, to explain the phenomena of aphasia, a "speech-motor path" from the cortical speech centre to the putamen, and a second "verbo-articulatory path" from the putamen through the globus pallidus to the crus and so to the pontine and bulbar motor nuclei. The probability certainly is that such a system is anatomically impossible.

On anatomical grounds the localization of "automatic movements" in the corpus striatum, or its description as a "subcortical motor centre" whose motor function is in any way analogous to that of the motor centres of the cerebral cortex, cannot be entertained. The independence of the motor cortex and the corpus striatum, and the peculiar projection-system of the latter, make these views untenable.

(2) Evidence derived from the sources of comparative anatomy and physiology has an important bearing on the function of the corpus striatum.

In the whole vertebrate series the corpus striatum is a prominent organ. Phylogenetically, it is a very old structure, consisting of the basal part of the telencephalon or fore-brain. In fishes it consists of a palæostriatum only, corresponding to the globus pallidus of the higher vertebrates: in reptiles and birds there are additions to it in the shape of (1) the archistriatum, corresponding to the nucleus amygdalæ of the apes and man, and (2) the neostriatum, which represents the putamen and caudate nucleus. The palæostriatum or globus pallidus is the oldest part of the corpus striatum not merely phylogenetically, but also ontogenetically. Its cells develop in the fœtus in mammals earlier than those of the other divisions, while the globus pallidus and the ansa lenticularis myelinate earlier than the fibres of the rest of the striatum.

The fibre-connexions of the palæostriatum are important. In all vertebrates a well-marked and definite bundle passes from the corpus striatum to the optic thalamus and beyond. As Edinger [19] says, a fibre-system found so universally and so obvious must have a special signifi-

[1] It should be said, at the same time, that Grünbaum and Sherrington [34] obtained no experimental evidence in the chimpanzee of the existence of a cortical centre in that animal analogous to Broca's area in man.

cance; it is, indeed, primeval (*uralt*). This basal bundle or basal fore-brain bundle (*basal Vorderhirnbündel*), a tractus strio-thalamicus and tractus strio-subthalamicus in one, is essentially striofugal or centrifugal, i.e., efferent or motor, and it links the palæostriatum to the optic thalamus and to the motor centres of the mid- and hind-brain and spinal cord. According to Johnston [40] this linking of the palæostriatum to motor centres situated caudally is effected by means of the fasciculus longitudinalis medialis (posterior longitudinal fasciculus), the oral end of which is continuous with the caudal extremity of the tractus strio-thalamicus. Thus the original motor pathway from the palæostriatum is broken once in the optic thalamus, and the fibres arising here probably make connexion with widely separated motor nuclei in the brain and spinal cord. Essentially the same motor conduction path, according to the same author, is found in all vertebrates, although its functional relations may be somewhat modified in mammals on account of the cerebral cortex. Whatever be the case in the lowest vertebrates, the posterior longitudinal fasciculus in the mammalia and in man cannot have the same function as its homologue may have had as a "primitive somatic motor fasciculus." The researches of Fraser [30] (cats and monkeys) show that only a few fibres unite the fasciculus to the optic thalamus, and these are all afferent to the thalamus or centripetal.

The facts are important by analogy, for they supply another instance of cerebral function moving away from its original localization with the development of the vertebrate species. Like the ansa lenticularis, the posterior longitudinal fasciculus has, in part at least, depreciated.

Edinger, however, does not describe the original tractus strio-thalamicus and tractus strio-subthalamicus (ansa lenticularis) as extending directly beyond the subthalamic nuclei and the substantia nigra in higher mammals; at the level of the posterior colliculi the bundle, important though it is, has disappeared. Van Gehuchten [31] has described an original "tractus strio-spinalis" following the course just mentioned, but it is not clear whether he considers the posterior longitudinal fasciculus its homologue, or whether he admits that the path is really indirect. He says it has not as yet been found in mammals, in which he believes it is replaced by the cortico-spinal path.

The researches of Ariëns Kappers [1] [2], de Vries [78], and de Lange [41], in the lower vertebrates, have shown that the palæostriatum is linked to the optic thalamus and mid-brain, medulla oblongata

and cord by double connexions, both efferent and afferent. Its relation to the trigeminal system in particular, both motor and sensory, seems to be very close. This is well seen in the reptilia. It is well recognized that the rule of double connexions between nervous ganglia obtains almost universally in the nervous system of vertebrates, so that while the main connexions of the palæostriatum are striofugal we cannot suppose that it is insulated from sensory stimuli in any way; on the contrary, we must conceive of the palæostriatum as a correlation-centre for various sensory impulses (olfactory, gustatory, &c.), from which passes caudally an efferent tractus strio-thalamicus, with connexions, for the execution of motor impulses. The part of the striatum associated with olfactory impressions is more particularly the archistriatum, the homologue of the nucleus amygdalæ in man. The archistriatum is connected with a tertiary olfactory path, and Ariëns Kappers thinks that even in mammals a part of the corpus striatum may subserve an olfactory function. However, be this as it may, the nucleus amygdalæ can readily be distinguished from the neostriatum (putamen and caudate) with which it is continuous only in appearance; its cell maturation is later than that of the palæostriatum and earlier than that of the neostriatum, and, as de Vries says there is doubt whether it may not really be pallial in origin, while Elliot Smith [72] has shown that at the palliostriate junction there is confusion owing to the rapid growth of (among others) the olfactory cortex in the neighbourhood of the corpus striatum, we may leave the archistriatum as not being of further interest for our subject.

Looked at from the point of view of comparative physiology, we may regard the original corpus striatum, in Elliot Smith's words, as that part of the original cerebral hemisphere whereby impressions of smell, and no doubt other sense impressions, may bring their influence to bear on the nervous mechanisms regulating movement.

The palæostriatum, then, has a projection-system which consists of the basal bundle, or tractus strio-thalamicus and strio-subthalamicus, and which is continued, according to Johnston, as the fasciculus longitudinalis medialis, or at least as a part of the latter; this is designated by him the primitive somatic motor fasciculus. It is therefore to be considered the homologue of the cortico-spinal paths of man, and is, for instance, in the fishes, the sole descending tract that can be compared to the cortico-spinal motor system of higher vertebrates.

With the progressive development of the brain the motor paths become more complex. When a pallium develops above the original

palæostriatum motor centre, as in reptiles, birds, &c., the descending paths are doubled. The earliest appearance of cortico-spinal fibres separating the two parts of the neostriatum and blending with the striofugal projection-system is in the higher reptilia, according to de Lange. The state of affairs in the bird's brain is particularly remarkable. In Ariëns Kapper's view it is possible that the neostriatum of birds acts vicariously for the neopallium or cortex. In the tractus strio-mesencephalicus are mingled fibres both of striate and of pallial origin, and the suggestion is made that it is because of the necessity for economy of space in the brains of birds that such a state obtains. It should not be forgotten, however, that McKendrick [48], Ferrier [22], Mills [52], and others have shown definitely that the pallium of birds is electrically inexcitable; Ferrier obtained no movements at all; McKendrick noted simply movements of the iris and eyeball. The mammalian brain, in its turn, is very different from that of the birds and reptiles. The reptilia have an olfactory pallium; birds a visual and an olfactory pallium; the lower mammalia, a visual, an olfactory, an auditory, and a tactile pallium. With further development of the pallium afferent systems are pushed beyond the level of the thalamus and corpus striatum to reach it; and while in response a definite cortico-spinal motor system is developed the primitive motor projection-system of the corpus striatum disappears, or, rather, is reduced to the ansa lenticularis, which does not extend beyond the nucleus ruber. Its function is replaced by that of the cortico-spinal or pyramidal tracts.

In some ways there is a parallelism between the development of the corpus striatum as a whole and that of the pallium. The former, consisting originally of a palæostriatum possessing motor and correlating functions, develops by the addition of a neostriatum (putamen and caudate) which is found for the first time in the lower reptilia and increases in relative size through the lizards, birds and mammals; so in proportion to the corpus striatum as a whole the pallium develops increasingly through the vertebrate series. ut the analogy does not carry us far; while the function of the pa...o-spinal system usurps that of the strio-spinal system we do not know that the neostriatum abrogates the function of the palæostriatum. In fact the exact relation of these two to each other in functional activity is far from clear, that is, in the case of animals whose pallium is still comparatively insignificant.

Indeed, the relation of the neostriatum to the palæostriatum is one of the difficult subsidiary questions in a difficult subject. Ariëns Kappers,

apparently, is the only investigator who has devoted attention to the matter. He believes that just as in the higher mammalia and man the pallium has taken the place of the corpus striatum as a whole, so the neostriatum (putamen and caudate) takes the place of the palæostriatum (globus pallidus) in birds. In his view, further, the connexions of the neostriatum with the thalamus is an indication that the former has functions in relation to the fillet and trigeminal systems. Whatever may be the case in birds, this view does not commend itself in the case of animals with a better developed pallium. My experiments in apes show conclusively that the neostriatum has no projection-system of its own beyond the palæostriatum; with the possible exception of a few caudate-thalamic fibres, the neostriatum is not connected to the thalamus or subthalamus at all; it is the globus pallidus which through the whole vertebrate series possesses the important projection-system. This may perhaps suggest that the corpus striatum should be considered as a physiological unit, or, rather that the functions of the neostriatum and palæostriatum are blended.

It will be understood from this brief sketch, then, that at one stage in the development of the vertebrates the thalamus and corpus striatum functioned as a brain in miniature, the latter being a correlating centre concerned with the translation of sensory into motor impulses; but, even at the best, its motor functions must have been simple compared with the complexities of the pallium of the mammalia. In the course of development the corpus striatum and its projection-system have depreciated; they have had to abandon their position of hierarchy in the field of motor activity. Thus the facts of comparative anatomy and physiology support the evidence derived from experiment. In view of the changing importance of the corpus striatum it becomes a delicate matter to allocate its function in the various animal groups; its function in man is not necessarily identical with its function in apes. Although the curious and unique features of the bird's brain demonstrate conclusively that evolution is not necessarily progressive, from the strictly motor point of view the corpus striatum seems to have been progressively shorn of its possessions; its proportionate size in man is less than in any of the lower animals, and it may be that the superman of the future will have no corpus striatum at all.

(3) We have seen that whatever function the corpus striatum once possessed there is no experimental evidence in apes to show that it exercises any motor function comparable to that of the motor cortex. There is no evidence to suggest that it is a centre for so-called automatic

movements. It is electrically inexcitable, and comparatively large unilateral lesions do not give rise to any unmistakeable motor phenomena. In short, the only proofs that it does possess a function of a motor order, in the widest sense, as we must say we should expect it to exercise in view of its phylogenetic history and the facts of anatomy, are to be obtained by a consideration of clinico-pathological data.

I have gone fully into the question of the physiology of the corpus striatum in man in my paper [82] on "Progressive Lenticular Degeneration," to which the reader is referred. It is unnecessary to recapitulate in this place; suffice it to say that in that paper arguments are advanced in support of the view that the corpus striatum is a structure which exercises a steadying influence, viâ the lenticulo-rubro-spinal projection-system, on the innervation, from the cortico-spinal or pyramidal system, of the "final common path"—the lower motor neuron, and that it is in a way concerned with the maintenance of "tone" of the skeletal muscles.

We owe to the genius of Sherrington [71] the conception of the "final common path." At the commencement of every reflex arc is a receptive neuron, which is reserved exclusively for impulses generated at one single receptive source. The motor neuron at the other end, however, receives impulses from many receptive sources. "It is the sole path which all impulses, no matter whence they come, must travel if they are to act on the muscle fibres to which it leads. Therefore, while the receptive neuron forms a *private path* exclusively serving impulses of one source only, the final or efferent neuron is, so to say, a *public path* common to impulses arising at any of many sources of reception." And again, "reflexes originated at different distant points, and passing through paths widely separate in the brain, converge to the same motor mechanism (final common path) and act harmoniously upon it. Reflex arcs from widely different parts conjoin and pour their influence harmoniously into the same muscle. The motor neurons of a muscle of the knee are the *terminus ad quem* of reflex arcs arising in receptors not only of its own foot, but from the crossed forefoot and pinna, and tail, also undoubtedly from the otic labyrinth, olfactory organs, and eyes. Thus, if we take as a standpoint any motor nerve to a muscle it consists of a number of motor neurons which are more or less bound into a unit mechanism; among the reflex actions of the organism a number can all be brought together as a group, because they all in their course converge together upon this motor mechanism, this final common path, activate it, and are in harmonious mutual relation with regard to it."

This illuminating conception of a "final common path" is not further applied by Sherrington in a detailed manner, but by implication it may be applied to the problem before us. The view which I hold of the function of the corpus striatum and its projection-system may be expressed as follows:—

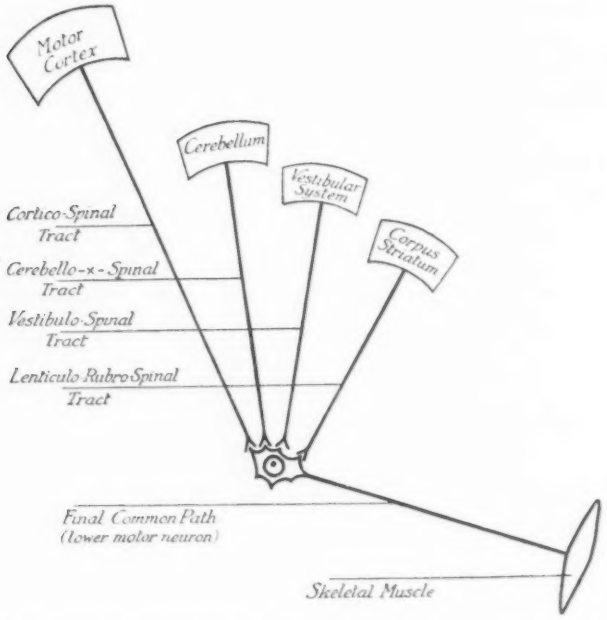


FIG. 26.—Diagrammatic representation of the various influences that act on the skeletal muscles viâ the final common path of the lower motor neuron.

Various influences act harmoniously on the final common path of the lower motor neurons: (1) The cortico-spinal motor system extends from the Betz cell "ganglion" to the arborizations round the anterior cornual cells, and its function is to innervate, or to conduct innervating impulses, originating we know not how in the cortex, to the final common path. If this system is impaired or destroyed by a lesion the result is paralysis. (2) The cerebellar system also exerts an influence on the final common path. Its ganglion is the cerebellum, from which it extends by a series of internuncial neurons to the lower motor neuron. The cerebellum exerts a co-ordinating and co-operating

influence on the stream of innervation passing from the rolandic motor ganglion viâ the final common path to the muscles. The routes by which cerebellar influence is exercised are complicated; some, perhaps, may pass by the tractus cerebello-tegmentalis to the opposite nucleus ruber and so back to the spinal cord on the same side; some travel by the superior cerebellar peduncle, contralateral optic thalamus and contralateral cortex and so back to the final common path by the cortico-spinal system itself. In this case the latter becomes an *internuncial* common path as opposed to the *final* common path, and Sherrington makes it clear that such internuncial common paths are by no means infrequent. For the sake of simplicity, however, we shall indicate cerebellar influence in our diagram by an independent path. A lesion of the cerebellar path results in inco-ordination or ataxia, or better, dysmetria, while there is no paralysis. (3) Another important reflex path carrying impulses to act on the final common path is the vestibular. It extends from Deiters' nucleus (to which there is a private path from the labyrinth) viâ the vestibulo-spinal tract to the anterior horn-cells. An additional allied mechanism is perhaps constituted by the posterior longitudinal fasciculus, which is linked to Deiters' nucleus and also passes to the anterior horn-cells. Interference with the function of the vestibular element in the activity of the final common path results in what is called by the French school "titubation." It is of course commonly held that some at least of the cerebellar influx to the cord is transmitted by Deiters' nucleus and the vestibulo-spinal path, and this may very well be so. But it is desirable to attempt to separate cerebellar from vestibular elements in co-ordinate innervation, and for diagrammatic purposes, at any rate, one may properly be distinguished from the other. (4) Finally, there is the strio-rubro-spinal path, conveying impulses from the corpus striatum, viâ the ansa lenticularis, nucleus ruber, and rubro-spinal tract, to the anterior cornual cells. In what way impulses originate in the corpus striatum is immaterial—they may depend on stimuli from the optic thalamus by thalamo-striate fibres; in any case, the evidence for the efferent action of corpus striatum impulses on the final common path, by the route just mentioned, is not to be lightly set aside. I have said that this influence is one which steadies pyramidal innervation along the final common path. In the absence of this influence tremor is likely to occur, and, as a rule, with increase of pyramidal action so will the tremor increase. It is an action-tremor. The reader is referred to my monograph for a full discussion of the evidence associating tremor

as well as hypertonicity of the skeletal muscles with defect of function of this internuncial system.

The accompanying diagram (fig. 26) indicates sufficiently, and in a graphic manner, the way in which I conceive the corpus striatum to act.

One or two questions remain for brief discussion. It may be asked, if this be the function assigned to the corpus striatum, and these the results of interference with that function, how is it I have been unable to obtain such symptoms in apes whose ansa lenticularis has been completely degenerated, or in whose corpus striatum large lesions have been placed? It may be said by way of response that the data mentioned above, in Section (2) of this chapter, will show how different are the anatomical relations and proportions of the pallium and corpus striatum in different animal species, and it will be understood, as has already been remarked, that the function of the latter structure in apes may not be identical with its function in man.[1] In fact the probability is that it is not identical. It should be borne in mind in this connexion that if the volume of the total encephalon be taken as 100, the proportionate volume of the basal ganglia is in man, 5; in the ape, 8; in the dog, 11; in the sheep, 14; and so on. That is to say, there are certainly structural differences in this matter between man and the ape. Again, there are undeniable physiological differences in the various animal groups, as far as the independent action of inferior and superior motor centres are concerned. Complete section of the cervical or upper dorsal cord in the frog does not diminish muscular tone in the limbs, according to Crocq [15]; in the dog there is momentary diminution of tone, which soon returns, but not quite to the same degree as before; in the ape, there is persistent and marked diminution of tone; in man, there is definite and complete abolition of tone. Analogous results are obtained when the motor area of the cortex is destroyed in these respective animals, as far as the region innervated by the destroyed cortical zone is concerned. Again, it is well known that the degree of recovery of movement after lesions destructive of the motor cortex in animals and in man varies considerably. After completely extirpating the hand area from the right hemisphere of a chimpanzee Grünbaum and Sherrington saw an immediate severe crossed brachioplegia, but it diminished rapidly, and in six weeks' time the animal had in large measure recovered the usefulness of the limb. In dogs and other animals lower in the scale the resulting paresis is even slighter and the recovery greater.

[1] It should also be noted that I did not allow any of my animals to live longer than three weeks, while there is a possibility that longer time should elapse after the lesion before the onset of tremor could be expected.

In fact, the expression "motor centres" conveys very different meanings according as we speak of one or other animal group. As Mills [52] has said, in the rabbit, cat and dog, for instance, the motor centres of the cerebral cortex are not on the same functional plane. And this is equally true of higher mammals. There are differences in the *organization* of the various motor centres, moreover: in man, to take but one example, all movements are not equally readily abolished by cerebral disease, or equally readily restored. It is possible to remove the entire cerebrum of the pigeon, yet it is capable of flight when thrown into the air an hour later. On the day of the removal of the cerebral centres from the limbs, a rabbit will jump vigorously. A week after removal of the crucial motor area, a puppy will walk, run, scratch, &c., as before. Obviously it is not the same with the monkey, still less with man.

These facts are mentioned simply to show that man is much more dependent on his motor cortex than are the lower animals, and they suggest—what indeed a consideration of the facts of comparative anatomy has already emphasized—that corresponding differences in the importance of the corpus striatum for motility are only to be expected.

The matter may be put in another way. In all the vertebrates there are higher and lower motor centres: in all, the latter are constituted by collections of grey matter in the cord and medulla and pons; the former are constituted by the corpus striatum in the lowest vertebrates, and by the motor pallium in the superior grades. The assertion is that the degree of independent action of the lower motor centres is greater in the less highly developed than in the more highly developed groups of the vertebrate series; the relation of the corpus striatum to its lower motor centres is different from that of the rolandic cortex to its lower motor centres. The corpus striatum, phylogenetically speaking, has never been a "lower motor centre," and in the event of cortical defect of function the degree of movement possible will depend on the organization of the lower motor centres, of which the corpus striatum is not one. In spite of the general similarities between the brains of the ape and of man, we cannot assume that a lesion of the corpus striatum in the one will result in the same disturbance of motility as is found with an analogous lesion in the other.

We have seen that in birds there *may* be a vicarious functioning of the corpus striatum for the motor pallium. The question arises whether in man any compensation for pyramidal failure may be possible

by extra-pyramidal routes. My own opinion is that this is extremely unlikely. We have neither anatomical nor physiological justification for such a hypothesis. The suggestion has been made by Probst [61] among others, that in the "Haubenbahnen" we have extrapyramidal paths capable of functioning for the pyramidal path. By these he means the tractus tecto-spinalis, rubro-spinalis, &c. They descend to the spinal cord from the mid-brain. But, in the first place, we have no anatomical knowledge of the way in which they might conceivably be reached from the motor cortex, except in so far as there is a fronto-rubral tract. Again, if compensation, of this kind be it noted, is possible, it should be met with constantly: this, however, is not the case. Permanent motor paralysis certainly occurs in man. As for the "centres" from which these descending "Haubenbahnen" arise, they are incapable, for anatomical reasons if for no other, of developing that capacity for complex and varied movement which would justify their being described as "lower motor centres."

The loose way of referring to "subcortical motor centres" in the basal ganglia and mid-brain is to be deprecated. We are using two different connotations of "motor centre" if we apply it both to the motor cortex and the nucleus ruber. The sole subcortical motor centres which exist are the columns of motor cells in the anterior cornua, with their bulbar and pontine homologues. There may be, and probably is, in man, a latent power of subsidiary development of adjacent (perhaps not necessarily adjacent) *cortical* areas and tracts to compensate to some extent for loss of pyramidal function; thus when a patient cannot write with his right hand, owing to a hemiplegia, he may learn to write with his left hand, or with his foot, or even with his nose he may indicate letters; in a case recorded by Bruce a completely paralysed patient affixed his "signature" to a document by holding the pen in his teeth and making appropriate movements with his head. Apart from this, however, a lesion of the pyramidal system in man entails permanent loss of certain movements—a state which does not appear to obtain in the ape. The degree to which the spinal cord is capable of automatic function has not yet been sufficiently investigated, so far as man is concerned, but it is known that in the lower animals—Goltz's [33] dog is a classical instance—the spinal cord achieves very much in the absence of the motor cortex. In that instance the corpus striatum, as well as the cortex, was removed [43]. Of old the Emperor Commodus decapitated his ostriches in the arena, round which they nevertheless continued to perambulate for a long time. It is probable that in man the sub-

cortical, *i.e.* medullary, motor centres do not possess, or rather retain, that faculty of independent action so characteristic of creatures lower in the scale. But there is no vestige of evidence, I repeat, that in man the corpus striatum is capable of assuming a long-lost function and of acting vicariously for the motor pallium. Its true motor function has gone, never to return.

One final question remains. Admitting that the corpus striatum has no longer any motor activity comparable to that of the motor cortex or of the spinal cord, and that its motor function is one of steadying (I purposely avoid using the difficult word "inhibiting") innervation as it streams along the final common path, is there any evidence to suggest that the organ under discussion has developed in other ways, and that it may be associated with innervation of non-striped muscle fibre? Does it bear any relation to organic, visceral activity? Has it to do with a central representation of the sympathetic and autonomic systems?

Langelaan [42] has put forward the hypothesis that the corpus striatum, with the body of Luys and the substantia nigra, is the highest motor centre for non-striped muscle. A great deal of attention has at different times been devoted to a consideration of the view that in the corpus striatum is a heat-regulating centre; also a respiratory centre, a vaso-motor centre, a blood-pressure and pulse-controlling centre, and so on. There are obvious difficulties in the way of accurately determining such functions by experiment, and the evidence hitherto adduced is far from convincing, besides being in some ways contradictory. The variety of animals operated on is also a very important complicating factor.[1] In my own experiments no evidence was obtained of any disturbance of respiration from stimulation or destruction of the putamen or globus pallidus in apes. And, further, the question must always remain, assuming any of these functions for the sake of argument, how are they carried out? Until we have clear anatomical proof of the connexion of the corpus

[1] It would make this paper much too long if one were to attempt anything like a complete résumé of these various investigations, the original descriptions of a large number of which have been perused. The unsatisfactory nature of much of the work has been clearly exposed by v. Beehterew [6], to whose chapters on the subject the reader is referred. Very briefly, the following are his main conclusions. (1) The corpus striatum (nucleus candatus) is not a centre for respiration; (2) nor for the vocal cords; (3) it has no influence on movements of the stomach and alimentary canal; (4) it has no connexion with the urinary bladder; (5) nor with the organs of sex; (6) it may have some association with the heart and blood-vessels by the vasomotor system; but similar experimental data are obtained from the optic thalamus; (7) it may have some connexion with the maintenance of body temperature, but how this is effected is quite obscure.

striatum with recognized bulbar centres, by direct or even intercalated neuronic communication, we cannot get any further in such matters. Such anatomical proof, as far as my knowledge goes, is not yet forthcoming.

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# ON APHASIA DUE TO ATROPHY OF THE CEREBRAL CONVOLUTIONS.

BY DR. G. MINGAZZINI.

*Professor of Neuropathology at the Royal University of Rome.*

SCARCELY ten years have elapsed since attention was drawn, first by Pick and subsequently by Dejerine and myself, to certain cases of aphasia which, as was proved by autopsy, were not caused by tumours or other diseases of the speech-zone, but were due to more or less severe atrophy of the respective convolutions.

Although the preceding observations have since been partially confirmed by other writers, nevertheless the literature dealing with this subject is still very scanty, and often consists of accounts of incomplete researches. For this reason, I have decided to publish the details of the following case, which I studied both during life and *post mortem* at the lunatic asylum in Rome.

Pio Marini, aged 59, a gilder. The patient, from his condition, is unable to give any information. He has never suffered from any infectious disease, or from syphilis, and has been moderate in the use of wine. About two years previously (1907), the first symptoms of the disease began to show themselves rapidly. These consisted in a tendency to impulsive actions, as well as in a difficulty in speaking and in understanding what was said. Those around the patient noticed that he gave the most curious names to the commonest objects (paraphasia); and that when his intimates did not understand him, and persevered in trying to ascertain his wishes, Marini could not comprehend their questions and broke out into threats and accesses of rage. The symptoms continued slowly and gradually to increase, without any signs of a stroke.

This state of affairs obliged the patient's relatives to send him to the lunatic asylum on March 1, 1909.

*The patient's condition, March* 10, 1909.—The eye movements, as far as they can be tested, are normal. In showing the teeth, the right upper lip becomes tremulous; the tongue can be fully protruded, and is slightly turned towards the left. The upper and lower limbs are able to perform all the usual active and passive movements, but, in producing the latter, the amount of resistance encountered is somewhat greater than the normal. The tendons and periosteal

reflexes of the upper limbs, and especially those of the lower limbs (patellar and Achilles tendons) are exaggerated. There is sometimes very evident foot clonus of the left side; the plantar reflexes give a flexor response. The abdominal reflexes are greatly exaggerated. A general hypalgesia is present. Speedy dermographia is evident.

*Condition, March* 12, 1909.—The patient remains quiet. At first he used to rave somewhat, and often called for a certain Don Antonio, who, according to him, ought to take him home; then he became calm, and showed himself indifferent. Echolalia is often noticed.

*Examination of the patient's speech.*—When questioned, the patient replies correctly only when asked his christian name and his surname. If other simple questions are put to him, he either repeats them (echolalia, or perseveration), or says: "Don Antonio"; "I do not know." He carries out verbal commands, provided they involve more or less common movements, with exactitude and rapidity; when, however, it is a question of obeying orders which are a little more complicated, he always replies "Don Antonio," and does not execute (does not understand) the order. He repeats words exactly. On being shown objects, and asked to name them, he succeeds at first (spoon, glass) and then replies as follows:—

| Q. | | A. |
|---|---|---|
| What is this called? | (a bottle). | Don Antonio. |
| ,, ,, | (an inkstand). | Marini Pio. |
| ,, ,, | (a pen). | Marini Pio, gilder; then, *I do not know*; then, *a paint brush*. |
| ,, ,, | (nose). | Nose (after touching it). |
| ,, ,, | (ear). | Ear (*idem*). |
| ,, ,, | (lips). | Chin. |
| ,, ,, | (a watch). | I do not know. |

When invited to read, he often repeats: "Marini Pio," or "Don Antonio." Sometimes, on beginning to read, the patient reads two or three words correctly, and afterwards reads some words in a quite mutilated manner, and then stops, puts down the book, and tries to induce the examiner to allow him to do something else.

*Written to dictation:—*

| | |
|---|---|
| Marini Pio. | Marini Pio. |
| Manicomio. | |
| Roma. | The patient always writes Marini Pio. |
| Roma. | |

*Copied.*—The sentence to be copied ran as follows: "Se avete dei dubbi sulla campagna elettorale del 'Messaggero' (if you have any doubts as to the electoral campaign of the 'Messaggero')." He wrote "Marini Pio."

*Condition, August* 5, 1909:—

| *Examination of Speech.* Q. | *Perception of Commands.* A. |
|---|---|
| What is your name? | Pio Marini. |
| Shut your eyes. | He obeys. |
| Open your mouth. | The patient does not open his mouth, but closes his eyes. |
| Stand up. | He obeys. |
| Sit down. | He obeys. |
| Raise your right arm. | The patient gets up and raises his left arm. |
| Get up, and go to the door. | The patient gets up, but does not go to the door. |
| Take the inkstand. | The patient does not obey the order. |

The patient thus understands part only of the commands. He often repeats the last words of the orders without understanding them (echolalia automatica), e.g., Stand up, he repeats: "Stand up" (and does not do so). Go to the window; he says: "Go to the window" (but does not obey). At other times he persists in using the same words: thus when shown different objects such as a pencil, a glass, spectacles, and asked their names, he always says: "Don Antonio."

*Condition, February* 12, 1910:—

| *Examination in the Comprehension of Speech.* Q. | *Perception of Commands.* A. |
|---|---|
| Shut your eyes. | He obeys. |
| Put out your tongue. | He obeys. |
| Stand up. | The patient does not obey, but says: "Don Antonio." |
| Give me your hand. | The patient raises both hands, but does not obey. |
| Shut the door. | The patient shuts his eyes. |
| Touch your ear. | The patient does not obey, and exclaims "Don Antonio." |
| Put on your cap. | He repeats: "Put on your cap," but does not do so. |

*Repetition of Words.*

| Q. | A. |
|---|---|
| Roma. | Roma. |
| Papa. | Papa. |
| Angelo (angel). | Angelo. |
| Repubblica (republic). | Repubblica. |

| Q. | A. |
|---|---|
| Uccello (bird). | Uccello. |
| Napoli (Naples). | Napoli. |
| Il mare è immenso (the sea is vast). | Immenso. |
| Il cielo è bello (the sky is beautiful). | The patient first repeats "il cielo," and, on the command being repeated, replies: "è bello." |
| La campagna è bella (the country is beautiful). | E bella. |
| Repubblica popolare (popular republic) | Popolare. |
| La casa è grande (the house is large). | This the patient does not repeat. |
| Circoscrizione (circumscription). | The patient repeats the word with some clear dysarthric disturbances. |
| Circondariale. | Circondariale. |
| Artiglieria (artillery). | Artiglieria? I do not know the word. |
| Circoncisione (circumcision). | He does not repeat the word. |

When several objects are placed before the patient, and he is requested to carry out an order, the results are as follows:—

| Q. | A. |
|---|---|
| Take the watch. | The patient obeys. |
| Take two soldi (two five centesimi pieces). | He does not do so. |
| Take the keys. | The patient does not obey, but exclaims "Don Antonio." |
| Take the scissors. | Idem. |
| Take the book. | Idem. |
| Take the inkstand. | Idem. |
| Take the bottle. | Idem. |
| Take the hat. | Idem. |
| Take the handkerchief. | He takes a ten-centisimi piece. |

When different objects are shown to the patient, and he is asked to name them separately, the results are as follows:—

| *Object shown.* | A. |
|---|---|
| A watch. | A watch. |
| A pair of scissors. | A pair of spectacles. |
| On making him take them in his hand. | I do not know. |
| A soldo (making him feel it). | I do not know. Don Antonio. |
| A pair of spectacles. | Don Antonio. |
| A bottle. | Don Antonio |

The patient thus showed signs of partial sensory aphasia, amnesia verborum, verbal paraphasia, paralexia, and almost complete agraphia.

*Condition, October* 18, 1910.—The patient is always taciturn: he spends the whole day in walking aimlessly about in a state of complete apathy, and takes no interest in anything around him. He cannot find his bed, the water-closet, does not know the hours of the meals, and at meal-time has to be put in his right place. He often eats with his hands, but when convenient he also uses a spoon. If a plate of soup is placed before him, the patient begins to eat with his hands, then he takes up his spoon properly, but nevertheless he eats now with his spoon, and now with his hands. He is not able to dress or undress himself properly: in dressing himself he puts on his trousers, and also his vest, and draws his shirt over the latter and buttons them correctly; then he takes his socks, and goes in this condition out of the dormitory to the first door he comes across. Sometimes when dressing himself he tries instead to take off his vest.

His spontaneous speech is reduced to the monotonous repetition of the words, "Don Antonio." When asked to read the sentence, "Senza pieta" (without pity), he reads "Aprile 30." When the request is repeated, he reads: "Piri piri, pi." When asked to read "Concorso ippico," he reads "Don Antonio." The patient is unable to read any easy written sentence, however short. He is also incapable of reading or recognizing single letters and numbers, or even a single figure. When asked to write out of his head, or from dictation, or to copy, he merely makes the following hieroglyphic, "m m."

*Comprehension of Questions.*

| Q. | A. |
|---|---|
| How old are you? | Don Antonio. |
| What is your name? | No reply. |
| To what country do you belong? | No reply. |
| What is your father's name? | No reply. |

Repetition: His spontaneous speech is reduced to pronouncing the words, "Don Antonio": he retains the capacity of repeating these words, although with decided dysarthric troubles: word-blindness and agraphia are complete, and word deafness is almost complete.

Voluntary movements of the face, the tongue and limbs, together with the tendon reflexes, were in the same condition as at the time of the preceding examinations.

The patient has a good perception of light when it comes from the right or left, but shows a certain fear if the light approaches too near his eyes.

*Condition, October* 23, 1910.—In the afternoon the patient suddenly began to run of his own accord, and fell down, producing abrasions of the skin on the right side of his face. As a rule, he only walks aimlessly about the garden, he does not recognize the refectory, the water-closet, or the dormitory, and always needs assistance in finding his own bed. In dressing, he is always

able to put on his vest and shirt properly, but is unable to get on his coat, unless the nurse puts it on his shoulders, when he manages quite well. Often, after putting on one shoe and sock, he goes out of the room and begins to walk about, carrying the other sock in his hand. As a rule, he does not

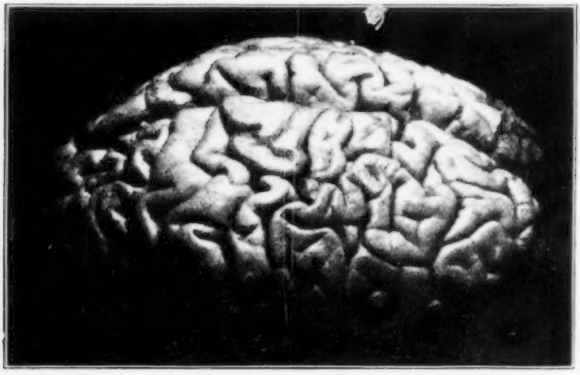

FIG. 1.—Photograph of the brain seen obliquely from above. Note on the right, the contrast between the enormous atrophy of the convolutions of the prefrontal lobe, and the normal volume of the rolandic convolutions.

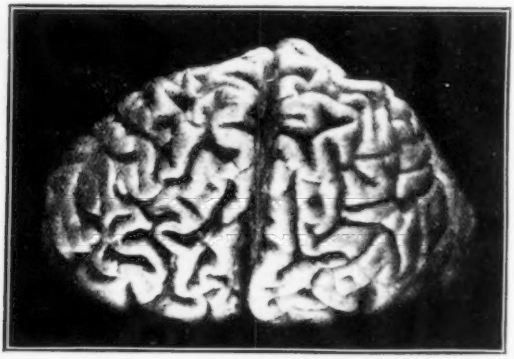

FIG. 2.—Photograph of the prefrontal lobes of the brain, seen from above. Note the enormous extent of the atrophy of the corresponding convolutions.

succeed in putting on both socks without the assistance of the nurse. Almost every morning, while sitting on his bed, he draws his socks over his hands, and then puts his hands into his shoes, then, however, following the suggestions and indications of the nurse, he finishes by putting on his socks and shoes properly. He eats, for the most part, with his hands, but when necessary he

manages his spoon well. At night he undresses himself properly and folds up his clothes neatly.

The late appearance and slow progress of the symptoms of aphasia, the absence of strokes or any focal symptoms, together with the ever-increasing

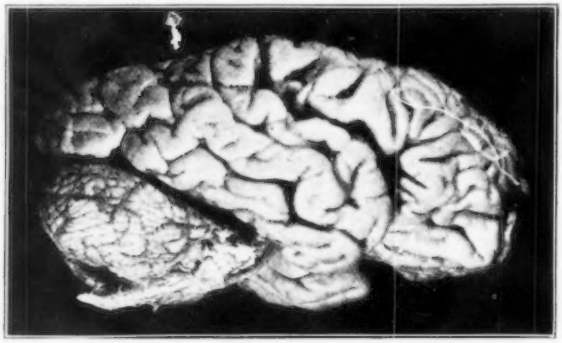

FIG. 3.—Photograph of the right cerebral hemisphere of the brain of the same patient. Note the conspicuous atrophy of the pars opercularis of $F^3$ and of the middle and posterior portion of $T^1$.

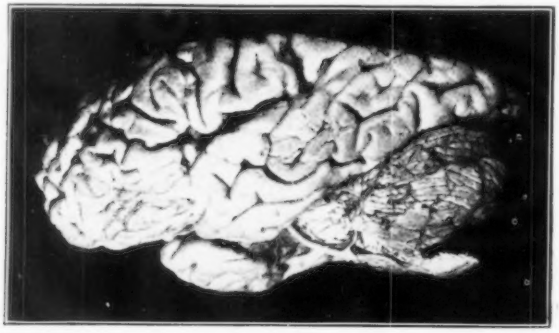

FIG. 4.—Photograph of the left cerebral hemisphere of the same patient. Note the serious atrophy of the pars opercularis of $F^3$ and of the middle portion of $T^1$.

dementia, led me to conclude that the patient was developing progressive atrophy of the cerebral convolutions, to which must be attributed the increasing speech defects. This diagnosis was confirmed by his death, which occurred on December 15, 1910.

*Autopsy.*—There is nothing amiss with the dura mater. The pia mater is normal and easily removed from the cerebral convolutions.

In the left hemisphere the frontal sagittal convolutions, especially the first and

second, the pars orbitalis and triangularis of the third frontal convolution have noticeably decreased in volume (fig. 1), and scarcely attain half of their normal size: they seem of an almost fibrous consistency to the touch. The median and posterior parts of $T^1$ and $T^2$, and especially the gyrus angularis, are somewhat diminished (figs. 1 and 4). The corresponding sulci are enormously enlarged. In the right hemisphere the præ-frontal (fig. 2) and temporal convolutions are

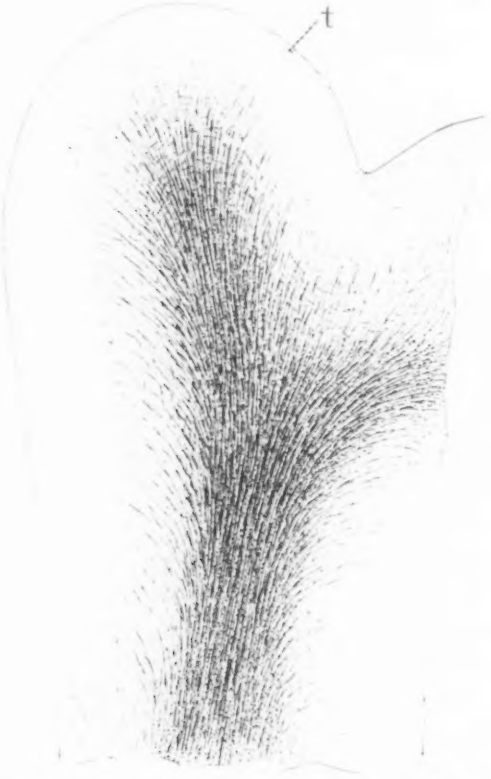


FIG. 5.—Section of the cortex of the left $T^1$. (Stained with Pal's haematoxylin.) *t*, tangential fibres. A very slight rarefaction of the fibres of the medullary axis is seen; the transverse fibres of the supraradial plexus are here and there slightly rarefied.

much reduced, although to a considerably less degree than is the case with those on the left (figs. 2 and 3). The median portion of $T^1$ is almost as much reduced as that of the corresponding convolution on the left side. In the zones where the convolutions are atrophied, the pia mater is raised here and there into little cysts containing a clear, serous liquid.

For the purpose of studying the condition of the cells, and the nerve-fibres of the cortex of the atrophied convolutions, and especially of those belonging to the acoustic and motor word spheres, I examined at measured points on the right and left, the pars opercularis of $F^3$ and the passage zone of the latter with the lower extremity of gyrus præcentralis and the median point of $T^1$. All these were stained either with Weigert-Pal's hæmatoxylin, or with hæmatoxylin-eosin.

FIG. 6.—Section of the cortex of the middle portion of the pars opercularis of the left $F^3$ (staining as above). Note the almost complete disappearance of the tangential fibres (*t*) and of most of the fibres taking part in the formation of the infra- and supraradial plexuses. In one part of the section (on the left of the figure) the disappearance of the medullated fibres is so nearly complete, that scarcely any traces of them are visible. The fibres of the medullary axis are so rarefied and degenerate that even in the most successful preparations they are conspicuous from their very pale colour.

In sections cut at the level of the zone of passage between the pars opercularis of the left $F^3$ and the lower extremity of the gyrus præcentralis (fig. 11), the nerve-fibres composing the medullary axis are very scarce, many are very thin and dilated from time to time in such a manner as to have an actual moniliform structure. The radial bundles taking part in the formation of the infra- and supraradial plexuses are attenuated, and the nerve-fibres accompanying them are broken and dilated: some of the transverse fibres have disappeared, almost all that remain are broken and dilated; very rarely the tangential fibres are replaced by a few swollen fibrils.

In the sections of the same zone stained with hæmatoxylin-eosin, the nerve-cells of all the strata show, to a greater extent than in the other convolutions examined, the alterations already described, the disappearance of a considerable number of these elements being especially noticeable (fig. 12, and fig. 9, *a*, *b*, *c*, *d*).

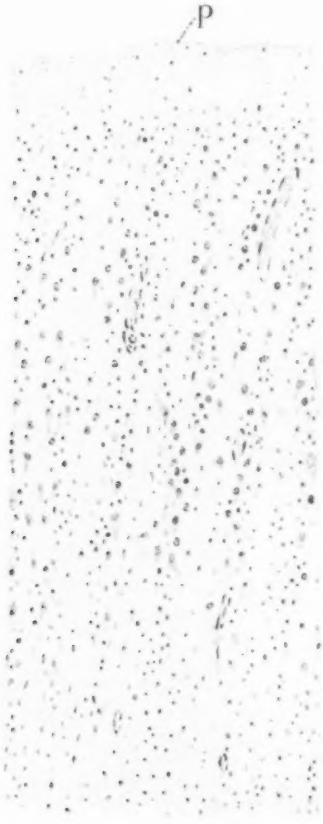


FIG. 7.—Section of cortex of the pars opercul of the left $F^1$ (stained with hæmatoxylin-eosin. Enlargement objective 4, ocular 2 Leitz); p, pia mater. A good number of the nerve-cells are present, and to much larger extent than in $T^1$; further, also here, there are but few which have kept their pyramidal form.

In sections cut on the level of the median part of the left pars opercularis of $F^1$ (fig. 6), the alterations of the medullary nerve-fibres described in the preceding sections are much more conspicuous. The fibres constituting the medullary axis, especially towards the dorsal (apical) half, are almost all broken during their course in such a manner that they are replaced by a number of little

masses and fragments (of myelin) which are arranged without any order (fig. 8). In the same way, the transverse fibres, and also the radial fibres making up the two plexuses, have disappeared in much larger numbers. The tangential fibres are reduced to a few irregular fragments occurring here and there. Here we observe the same alterations of the nerve-cells as in $T^2$. The number of those preserved, however, is relatively larger (fig. 7, and fig. 9, *c*, *d*).

In frontal sections of the cortex of the median part of the left $T^1$ there are, in the medullary axis of the Pal preparations, numerous small bundles of well-preserved fibres (fig. 5), though here and there a fair number of degenerate medullated fibres occur, and small masses and drops of myelin. Also in the infra- and supraradial plexuses a good number of fibres have been preserved;

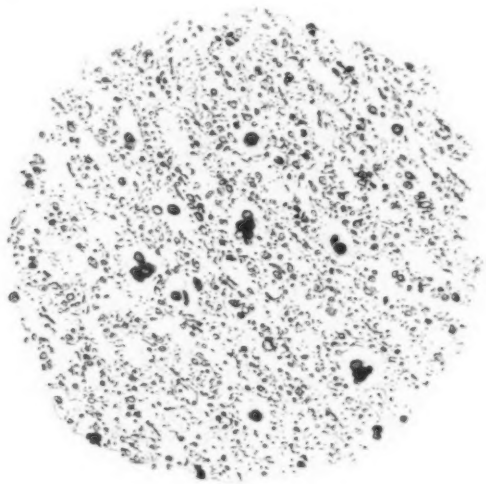

FIG. 8.—Segment of the medullary axis of the pars opercularis of the left $F^3$. Much enlarged. (Enlargement, objective 6·7, ocular 4 compens., Leitz.) In the place of the radial nerve-fibres running longitudinally are seen numerous little blocks of myelin, which are more or less dilated, and separated from one another by large clear spaces.

nearly all of these have, however, a moniliform structure owing to their having become dilated during their course. The tangential fibres are, to a great extent, preserved. In the hæmatoxylin-eosin preparations the following facts are observed; a considerable number of nerve-cells are seen to have disappeared, (fig. 10), and in almost a uniform manner in all the strata. In those which have still been preserved are clearly seen the nucleus with its network and nucleolus, in many the cytoplasm is almost completely filled with granules of a yellow pigment; in others the cytoplasm has in a great measure disappeared and only stains slightly (fig. 9, *e*, *f*). Thus, not a few of the pyramidal cells seem as if truncated, while in others the surrounding

protoplasm has completely disappeared, and it is not always easy to distinguish the nucleus of the nerve-cell from the nuclei of the glia. The fibres and the cells of the glia are normal in number, only on the periphery of the cortex of the said convolutions are the bundles similar in their thickness and shape to those described and figured by Franceschi. Thus there is not always a

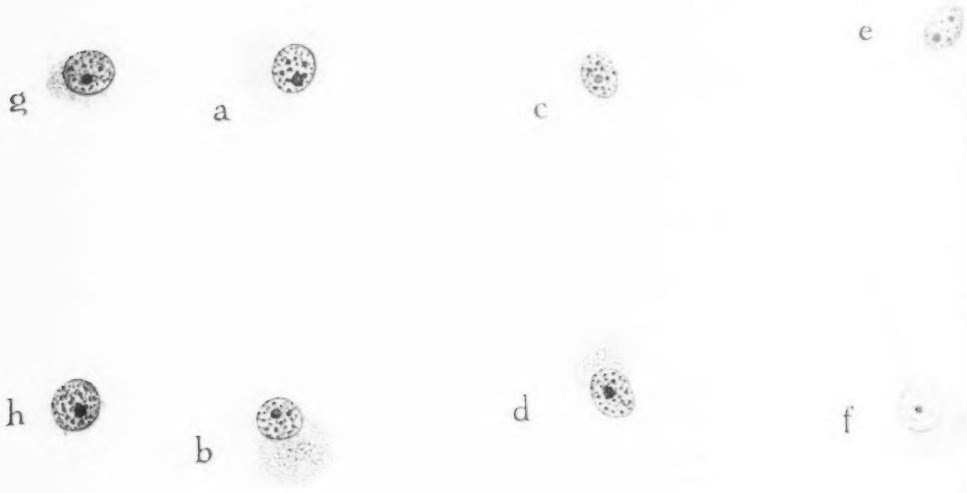


FIG. 9.—Types of nerve-cells of the cortex of the convolutions belonging to the motor word and to the auditory speech zones of the left side. Stained with hæmatoxylin eosin. (Enlargement, Leitz, ocular, compens. 4, objective 1½ min.). *a* and *b* are nerve-cells belonging to the cortex of the passage zone between the pars opercularis of left $F^3$ and the gyrus præcentralis, in which the cytoplasm has in part disappeared; *b*, nerve-cells (pyramidal), in which the cytoplasm is in a great measure invaded by granules of yellow pigment; *g* and *h* are nerve-cells belonging to the same convolution, the cytoplasm has almost completely disappeared; *c* and *d*, pyramidal nerve-cells from the cortex of the pars opercularis of the left $F^3$; in *c*, the cytoplasm is slightly coloured; in *d*, the yellow pigment occupies a great part of the latter; *e* and *f*, nerve-cells belonging to the cortex of the left $T^1$; in *e* the cytoplasm has in part disappeared, and the prolongations appear as if truncated; in *f* the cytoplasm is, to a large degree, invaded by the yellow pigment.

correspondence between the changes in the nerve-cells, and those which have taken place in the medullary fibres, and in fact, while in the pars opercularis of the left $F^3$, the changes in the fibres are very great, those in the nerve-cells are relatively little noticeable. On the other hand, in the passage zone between the left $F^3$ and the gyrus præcentralis, the nerve-cells present extremely noticeable alterations, while the medullary nerve-fibres, though certainly changed, are altered to a much slighter extent.

In the right $T^1$ there is no appreciable reduction of the nerve-fibres of the medullary axis, nor in those of the supra- and infraradial plexuses; the tangential fibres are also but little reduced, although fairly numerous varicose dilatations of the latter occur occasionally.

In sections at the level of the passage zone of the pars opercularis of the right $F^3$ to the adjacent part of the gyrus præcentralis, the medullary nerve-

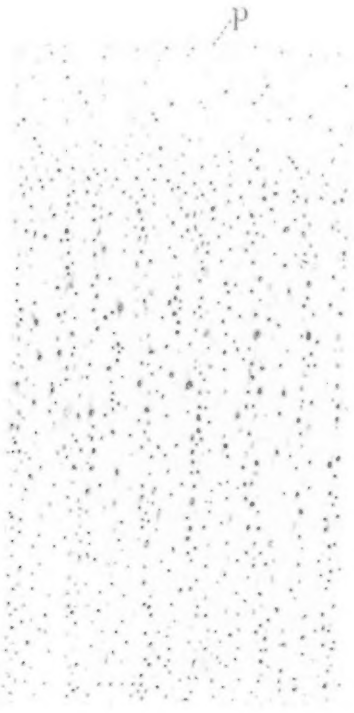


FIG. 10.—Section of the cortex of the left $T^1$ (stained with hæmatoxylin-eosin, enlargement objective 4, ocular 2, Leitz). Note the disappearance of many nerve-cells of the different strata of the cortex; the nerve-cells, especially the pyramidal ones, have to some extent lost their characteristic shape, owing to the loss of a considerable portion of the cytoplasm.

fibres appear to be well preserved, only some rare varicose swellings are seen in the tangential fibres, and in some of the vertical fibres of the infra- and supraradial plexuses.

In the pars opercularis of the right $F^3$ (fig. 13), the changes are greater than in the other two zones, many of the tangential fibres have disappeared, while in these, and also in the transverse fibres, numerous varicose swellings

occur. In the fibres of the medullary axis the disappearance of some fibres is noticeable.

In the nerve-cells of the right $T^1$ most of the cytoplasm has disappeared, and a few only of the cells are missing, although a larger number have disappeared in the sections of the passage zone from the right $F^2$ to the gyrus præcentralis, and still more in the pars opercularis of the right $F^3$.

FIG. 11.—Section of the cortex at the point of origin of the left $F^1$ from the lower extremity of gyrus præcentralis (stained with Pal's hæmatoxylin). The tangential fibres, and those forming the infra- and supraradial plexus, are much rarefied; the same is seen in the medullary axis, and especially in the basal portion of the latter.

## SUMMARY.

In the period between 1907 and 1909, the patient showed disturbances in his speech, which gradually increased, and consisted in the use of unusual words in ordinary conversation (paraphasia and echolalia). He also experienced difficulty in understanding many questions. After

two years (March to August, 1909), the examination of the patient revealed true partial sensory aphasia (with automatic echolalia and perseveration), associated with paralexia and almost complete agraphia.

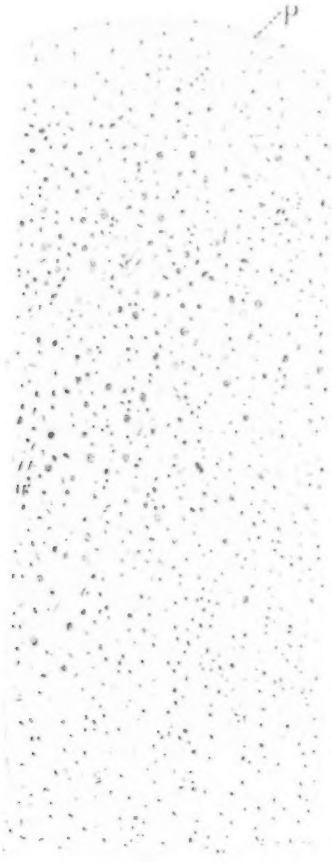


FIG. 12.—Section of cortex at the point of the passage from the pars opercularis of the left $F^3$ to the adjacent portion of the gyrus præcentralis. (Enlargement and staining the same as in figs. 7 and 10). The disappearance of the nerve-cells is much more noticeable than in the two sections 7 and 10, the pyramidal nerve-cells preserved being very few.

In February, 1910, the sensory aphasia had become almost complete and some dysarthria was noticed in his repetition of words. The understanding of words was extremely limited; further, a condition of advanced dementia showed itself, accompanied by symptoms of agnosia.

In October, 1910, the speech disturbances had become still more serious; the word deafness, the alexia and the agraphia were complete, while voluntary speech was almost entirely absent. Parallel with these

FIG. 13.—Section of the cortex of the pars opercularis of the right F³ (stained with Pal's hæmatoxylin). The medullary fibres are well preserved, except for a slight rarefaction of the fibres of the supra- and infraradial plexus, and on one side only of the section.

progressive disturbances of speech a condition of mental weakness gradually developed, which at last became a true dementia and was attended with symptoms of agnostic apraxia, and psychical blindness.

Two months later (four years after the beginning of the disease) the patient died.

The *post-mortem* revealed severe atrophy of the prefrontal and temporal convolutions, the left side being the most affected, while the histological examination showed severe alterations in the nerve-cells and medullary fibres of the convolutions belonging to the Broca region (*in sensu lato*) and to $T^1$, these changes being greatest on the left side.

## Critical Considerations.

Having thus described this new case, it will be well to compare its clinical and anatomical features with the results obtained by other writers. The complex of symptoms is almost uniform, and consists of a double set of phenomena, of which one belongs to speech and the other to the mental processes.

In the case described by Bischoff, the power of understanding words was extraordinarily impaired, but that of the repetition of words was quite intact. At the autopsy, atrophy of both the temporal lobes was revealed, the left one being the most affected.

Liepmann's patient was able to speak spontaneously, though intercalating clear signs of paraphasia. He understood questions, but he first repeated them in an interrogatory form, and then replied. As the disease progressed, the patient no longer understood the sense of the words, which he still repeated, though without giving any reply (automatic echolalia) and his command of spontaneous words became much reduced. Macroscopic investigation revealed atrophy of the frontal and temporal convolutions, and especially of the apex of the left temporal lobe; the smallest of all were the left $T^1$ and $T^2$. Upon the pia were vesicles containing a clear liquid.

In their first case of aphasia, P. Marie and Léri did not record any appreciable alterations in the horizontal sections of the right hemisphere, the lateral ventricle was found to be dilated, and especially the upper portion of the occipital pole. In the subependymal region it seemed to be surrounded by a sclerotic zone, and the white matter of the hemisphere appeared much atrophied. In the cortex of the brain there were no lesions whatever.

In the second case of the same writers, where the patient was affected with typical sensory aphasia, abnormal dilatation of the left occipital cornu was also found.

In a case of Ascher's, which was not typical, inasmuch as motor

aphasia, first temporary and afterwards permanent, was associated with paralytic dementia, there were found the usual lesions of this psychosis, further in the left $T^1$, the degeneration of the nerve-cells and of the white matter had reached a more advanced stage than in the rest of the brain.

In Shaw's case, the aphasic symptoms, consisting of word-blindness and word-deafness, suddenly manifested themselves; the patient was suddenly seized with paralysis of the right arm. The affection afterwards disappeared, but thenceforward the patient was afflicted with a slight incoherence of speech, and in addition showed signs of word-blindness and word-deafness. At the autopsy, atrophy was revealed of both the gyri angulares and of both the $T^1$ and $T^2$. This case is, however, exceptional, and it is very doubtful whether these disturbances of the speech were present before the occurrence of the stroke.

In Mills's case, where we have to do with a man who had suffered from complete word-deafness for thirty years, without any improvement in his condition, it was found at the *post-mortem* that there was considerable atrophy of $T^1$ and $T^2$ on both sides, but chiefly on the left.

In Edlich's patient, a change was first noticed in her character and manners, together with a reduction in her command of words; afterwards real motor aphasia gradually developed, associated with sensory aphasia, which was incomplete at first, but afterwards became complete, and was accompanied by agraphia and total alexia. The patient only showed signs of sensory apraxia. In the last stage of the disease, the patient's conduct was increasingly insane; she no longer recognized persons and rooms, wandered about aimlessly, rose at night, and displayed a marked tendency to laughter and tears. At the autopsy, the weight of the brain was found to be reduced to 893 grm. This decrease in weight was due to advanced atrophy of both the frontal lobes, while in the corresponding sulci the pia formed cysts as large as a hazel-nut. The parts most atrophied were the posterior portion of $F^3$ and the left insula.

In my case, No. 1 (published in 1902), which was that of a woman (illiterate), aged 67, the first symptoms appeared after a slight stroke; they consisted in in slight dysarthric troubles (the patient pronounced words badly and scanned them), in a reduction in her command of words, and in a slowly progressive incapacity for understanding the meaning of words. These symptoms continued to increase slowly; thus, a few months before her death, the patient did not understand a single word, and could only pronounce certain syllables (be, be, po, po, pa)

During this period, she performed foolish acts due probably to agnostic apraxia. She put her dress over her jacket, exchanged her spoon for her fork or knife, burst into laughter or tears without any reason. Examination revealed increased resistance in the limbs to passive movements. Reflex iridoparesis to the light, mostly on the left. Macroscopic and microscopic examination showed that the convolutions were reduced in volume, and that their external surfaces were shrivelled and dark in colour, especially on the left. The cerebral hemispheres were full of liquid. The grey matter of the cerebral cortex and of the cerebral ganglia were of a darker colour than usual. The weight of the encephalon was 1,000 grm. Histological examination (Nissl's technique and method) revealed a considerable amount of alteration in the nerve-cells of all the strata of the cortex, and especially in those of pyramidal shape. In the pars opercularis of the left $F^3$, a fair number of the nerve-cells were affected by a diffusion of pigment; in many, a good deal of the cytoplasm had disappeared, while some cells showed the characteristics of chronic alteration. In the lip of the calcarine sulcus and in the left $T^1$ alterations in the nerve-cells were relatively rare.

In the patient studied by Alzheimer there gradually developed, first motor aphasia, then partial sensory aphasia and lastly word-deafness. At the *post-mortem*, $T^1$ and the lobulus parietalis inferior were found to be darker than is normally the case. Microscopic examination revealed in these, degenerated convolutions, sclerosis and calcification of the nerve-cells, containing both large and small nuclei poor in chromatin. The medullary fibres of the corresponding cortex had disappeared. At the same time, in some of the brown spots of the above-mentioned convolutions, a large number of enormous pyramidal cells had made their appearance.

Veraguth's patient manifested, for a short time, symptoms referable to the subcortical form of sensory aphasia. Words sounded to him like a murmur, while his spontaneous speech was fluent and free from mistakes. At the *post-mortem*, there was discovered to be a considerable degree of atrophy of the posterior portion of the pars opercularis of the left $F^3$, and also of the median portion of the left $T^1$; these zones were reabsorbed and their places taken by a serous liquid. No microscopic alterations were met with in the injured part.

In Franceschi's patient a relatively short period of depression was succeeded by sufficiently clear symptoms of sensory aphasia, together with signs of extreme dementia. The latter revealed itself both in serious lapses in behaviour, and in the fact that the woman was unable

to answer questions coherently. Neurological investigation disclosed cutaneous hyperalgia, loss of the plantar reflexes and exaggeration of the patellar and Achillis reflexes (without clonus). There was noticeable atrophy of the three left temporal convolutions. In the cerebral cortex corresponding, many nerve-cells had either disappeared, or undergone alteration, this being especially the case with the pyramidal cells. In the zones whence the nerve-cells had disappeared, there were many glia elements, both in the grey and the white matter. A slight rarefaction of the radial and of the transverse nerve-fibres was also recorded, together with an absence of the tangential fibres. These alterations were much less evident in the right temporal convolutions.

Pick studied three cases of the kind. The first was a woman, aged 58. The disease had begun two or three years before with symptoms of dementia in the form of loss of memory and serious loss of the power of identification; she believed that her son was one of her nephews, that the house she inhabited was her own property, &c. Upon this, followed an actual loss of all capacity of orientation; the patient no longer knew the time, and could not find her way to church. An examination, made at this time, revealed difficulty in finding words and in understanding their meaning. Thus, the patient was incapable of understanding the sense of words, but she repeated them correctly and in the form of a question. Two years later, the dementia had made rapid progress, and the patient no longer comprehended any questions, while her command of words was reduced to the use of a few stereotyped phrases.

Pick's second case was that of a woman, aged 75, who had already been ill for three years when she came under his observation. She began to show signs of want of power of orientation, pulled up the vegetables in the garden and went out of her house for no purpose. Her comprehension of questions was most limited, so that she gave one the impression that she had become almost deaf. She could write well if she copied (servile writing). Some months later, the disturbance of her speech became more serious; a jargon-aphasia prevailed, both in her spontaneous speech and when she named objects. Her command of words had continued to become more limited, with a tendency to the repetition of the same phrases.

The third case was that of a woman aged 38, suffering from progressive paralysis, in which numerous oculo-motor disturbances were accompanied by hypokinesis of the lower branch of the seventh right nerve and noticeable dysarthria and exaggeration in the patellar reflexes.

The investigation of her speech revealed the presence of paraphasia (of the verbal and syllabic type), less evident during emotion. But the dominant symptom was amnesia verborum; the patient when asked to name an object always replied "I do not know what it is."

At the *post-mortem* of the first case was found a considerable atrophy of the convolutions, and especially of the left frontal and temporal gyri. In the second case, the atrophy of the encephalon was so great that its weight was reduced to 967 grm. The affection extended to all the convolutions, but was most marked in the left temporal lobe. The condition of the third case was almost identical.

In my present case (No. 2), the patient began first to show signs of partial word-deafness, which were very soon followed by symptoms of agnostic apraxia, amnesia verborum, paralexic troubles, and almost complete agraphia. Later, the sensory aphasia became complete, and was associated with dysarthria in repetition; while the patient's command of words became increasingly limited, and the dementia increased. At last, the agnostic disturbances became extreme, the pre-existing symptoms of aphasia became aggravated and more evident, while the patient's spontaneous speech became reduced to the repetition of the stereotyped words "Don Antonio," and complete loss of comprehension of words and total agraphia followed.

The *post-mortem* revealed a considerable amount of atrophy of the prefrontal lobes, especially of the pars opercularis of the $F^2$, and of the upper temporal convolutions, the left being more markedly affected than the right, and particularly in the middle portion. Microscopic examination of the cortex of the more affected convolutions showed the presence of a true process of degeneration affecting the nerve-fibres of the medullary axes, the superior and inferior plexuses and the tangential fibres; the nerve-cells of the cell strata of the cortex were severely altered; the nerve-cells of the motor word area had suffered more than those of the auditory word area; and those on the left side were more affected than those on the right.

The symptoms of the Dejerine and Sérieux case coincided (Liepmann) with the complex of transcortical sensory aphasia, all the more since difficulty in reading and writing were uncommon. The Dejerine-Sérieux patient, in fact, was affected by a slighter degree of echolalia, namely, in the form of asking questions, and did not get as far as subcortical sensory aphasia (Pick). Further, the essential feature of this last type of aphasia is that speech is not apprehended as such, and therefore is neither understood nor repeated, while the other speech

functions are intact. In Dejerine's case, on the other hand, the patient repeated the questions, although, as a rule, he did not understand the sense. In writing from dictation, he was faithful to the sounds of the words, and the chief mistakes were those which anyone (writing) would make, through failing to understand the sense of what was dictated. At the *post-mortem* was found symmetrical atrophy of the temporal lobes, which above and before were reduced to half their normal volume, so that the insula was exposed. Their cortex had more consistency than that of the rest of the hemispheres; the pia was adherent, microscopic examination revealed the disappearance of the tangential fibres of the nerve-cells of the molecular strata, of the fibres of the radii and the short association fibres, as well as a decrease in the number of the pyramidal cells, especially in that of the small ones.

Rosenfeld's first patient (a man, aged 62) was sufficiently correct in behaviour during the early stage of the disease, but he was less active and played chess all day. His powers of reading, writing spontaneously, of copying, and of understanding and speaking spontaneously were perfect. With the passage of time (eight years) his power of criticism weakened, as did also his capacity for association of ideas. The neurological examination carried out one year before his death (i.e., when he was received into the hospital) showed that the motion and reflexes, &c., were normal; verbal amnesia was very noticeable; he was able to read and to write from dictation. On the occasion of a second examination it was observed that the conditions of speech were unchanged, though he uttered few words spontaneously. The speech disturbances remained the same until the patient's death, which took place one year later. At the *post-mortem* the left temporal lobe was found to be much reduced, the atrophy having chiefly affected $T^2$ and $T^3$. $T^1$ was relatively larger than either of the latter. The convolutions (including the apex) of the right temporal lobe were smaller than normal. Microscopic investigation showed that in the medullary zones, which were much reduced, the perivascular lymphatic spaces were notably dilated, and that an enormous number of nerve-fibres had disappeared from the cerebral cortex. The number of the ganglion cells were greatly diminished, but they had mostly preserved their fibrillary structure; the nucleus was, in general, well preserved; it was surrounded by a granular substance.

In Stransky's case it was noted that the patient could not understand the sense of many words, and showed a tendency to reply, repeating first the question addressed to him (not automatic echolalia),

but evinced little inclination to speak spontaneously. He could repeat correctly what he heard, and also some songs, but nothing else at will; he also showed, in general, a tendency to word-perseveration. He used to read aloud, but with evident paralexia, and he did not clearly understand what he read. He was incapable of writing, and even of copying. Flexibilitas cerea was evident. The patient was unable to recognize the use and significance of the commonest objects. He manifested a tendency to echopraxia, servile imitation of what he saw others doing. At the *post-mortem* atrophy was found to be present, especially on the left side, some special parts of the cerebral convolutions being affected, i.e., the middle part of gyrus calloso-marginalis, the cuneus, the praecuneus, and, above all, gyrus supra-marginalis; the atrophy of the said zones on the right was much less noticeable.

As a general conclusion we find that aphasic disturbances are not always uniform. In some cases the prevalent symptom is perceptible even to lay minds, as it consists in an incapacity to comprehend the meaning of words and of a considerable number of questions, and it manifests itself early. Gradually, the disturbance becomes more and more noticeable, and finally the patient becomes indifferent to all questions. In the development of aphasic troubles, occasionally the intervention of true paraphasic troubles, of the verbal and syllabic type, has been recorded, sometimes amounting to jargon-aphasia, or perseveration. Dysarthric disturbances are of rare occurrence (in Pick's first case and in my patients No. 1 and No. 2).

Sometimes the patients, though understanding the questions, repeated them before replying (simple echolalia); with the progress of the disease, this echolalia always assumes the automatic form, for the patients repeat the questions, almost as if obliged, though they do not understand their signification. With sensory aphasic disturbances are often associated, from the commencement, difficulties in recalling and pronouncing words. Occasionally these symptoms precede the sensory aphasia. The first signs are an incapacity for finding words—amnesia verborum—which later on gives place to a progressive reduction in the command of words, and also to an incapacity for repeating pronounced words. This trouble always increases with time, so that finally every effort of the patient to speak merely results in the utterance of one or two words, or of some syllables (in my first case the patient said be, be, po, po, pa, pa) or at most a few stereotyped phrases (Pick's cases 1 and 2, my case No. 2). In a few cases it is almost impossible to judge whether the progressive aphasia proceeded

parallel with the loss of the memory of the words, or if it was only consequent on an inability to recall the motor images of an always greater number of words.

Many of the patients examined were illiterates, which accounts for the lack, in the greater number of cases, of notes respecting their capacity for reading and writing. In rare cases, the power of reading and writing remained unimpaired throughout the course of the disease. As a rule, the patients at first understood what they read, but made mistakes when reading aloud (paralexia), but they always finished by being unable to pronounce the words they read, much less could they understand them (word-blindness). Sometimes the capacity for writing was partially retained: the patients could write to dictation and could copy. Sometimes difficulties in writing (servile writing) showed themselves, either at the beginning or during the progress of the disease, and generally increased almost parallel with the development of the sensory aphasic troubles, so that in the end the patient was unable to write at all.

Parallel to the aphasic disturbances, disorders of the other mental processes developed. At the beginning of the disease the patients neglected their business, became less efficient, and showed less capacity for work, and above all, their critical faculty became weakened. With the progress of time they forgot things to an enormous extent, seemed to have no idea of time or of place; they were unable to distinguish persons, and no longer recognized the faces of their friends or the aspect of rooms, but wandered about aimlessly, arose during the night, pulled up plants in the garden, and no longer knew how to dress themselves, sometimes putting on only one shoe or one sock. Sometimes they showed actual signs of dyspraxia, usually of the agnostic type, putting a dress over a jacket, using a spoon instead of a fork, putting socks over their hands, perhaps in consequence of partial psychical blindness. This symptom-complex is always completed by exaggerated emotion which culminates in spasmodic laughter or tears (Edlich's case) usually without adequate cause (my case No. 1.)

Paralytic symptoms rarely manifested themselves during the course of the disease. In my case, No. 2, there was slight facio-lingual-brachial hypokinesis with an exaggeration of the tendon reflexes of both sides and sometimes with clonus of one foot. In Shaw's case partial paralysis of the right arm is recorded; this, however, afterwards disappeared. In Liepmann's patient there was, in addition to a slowness in pupillary reaction, a tremor of the hands and tongue. The patient walked insecurely, and with his legs far apart.

The age at which the disease declares itself varies from 38 to 67; it attacks men and women about equally. Its course is rather slow and progressive, the exact date of its beginning is difficult to determine. In general the disease lasts from two to eight years, with an average duration of four years. Mills alone states that in the case of his patient the malady had lasted for thirty years.

As for the macroscopic and microscopic data recorded by the various writers in studying their cases, it can be stated that the fundamental change consists in an atrophy of the cerebral convolutions, and that the atrophy is not uniform, either as regards the different lobes affected or as regards the right and left halves of the brain. The alterations are generally more pronounced on the left side. In some cases there occurred a dilatation of the lateral ventricle, especially of the occipital cornu (Marie's second case). Occasionally this dilatation is associated with atrophy of the medullary matter of the hemispheres, and with sclerosis of the subependymal region (first case of P. Marie and Léri). At other times it is a question of an atrophy of all the cerebral cortex (my case No. 1), but chiefly of the left $T^1$ (Ascher's case, Pick's second case), or else the atrophy is limited to one part of the parietal and temporal lobes, i.e., to the gyri angulares and to $T^1$ and $T^2$ (Shaw), to both $T^1$ and $T^2$ (Mills), to the supramarginal gyrus, to the cuneus and to the præcuneus (Stransky), to the upper and anterior portions of the temporal lobes (Dejerine and Sérieux), or to the three temporal convolutions, especially the left (Franceschi). Sometimes the atrophy affects the frontal convolutions as well as the temporal (my case No. 2 and Pick's cases 1 and 3), or the frontal convolutions of both sides, and the left insula (Edlich).

The histological examination of the cortex of the atrophied convolutions, which has hitherto seldom been made, reveals varicose swellings of the fibres and almost always the disappearance of many of the transverse fibres of the infra- and supraradial plexuses. Almost without exception a greater or lesser number of the nerve-cells have disappeared in an almost regular manner from all the strata. Nearly all the nerve-cells which have been preserved show signs of pronounced modification, which consists in the pigmentation and reabsorption of the cytoplasm. Occasionally an increase was observed in the cells of the glia of part of the atrophied convolutions. A parallelism does not always exist between the alterations of the medullary fibres and those occurring in the nerve-cells (my case No. 2).

In Alzheimer's case the nerve-cells had undergone degeneration

and were sclerotic and calcified; the nuclei were poor in chromatin and there were giant pyramidal cells at the same level in some of the convolutions, which were of a darker colour than normal. It may be said, briefly, that the lesion causing the aphasic symptoms consisted of an atrophy, which rarely extended to the whole cerebral cortex, but was limited, although not exclusively, to the temporal convolution, or else to the frontal lobes, usually the left one. The corresponding histological alteration resolves itself principally into a primitive degeneration of the nerve-cells and medullated fibres of the grey matter of the cortex, and of the axis of the convolutions.

The reasons that atrophy at one time attacks all the cerebral cortex, and at another only affects certain parts, are at present quite unknown to us. It is impossible to conceive that this difference of behaviour can depend upon the method of the distribution of the arteries, for this hypothesis would not explain why the disease sometimes spares the gyrus præcentralis, or why the middle of the gyrus temporalis supremus is much more frequently attacked than the extremity. Sometimes an evident parallelism can be observed between some of the aphasic disturbances and the seat of the macroscopic cortical changes. In those cases where the sensory-aphasic symptoms are dominant (Mills, Bischoff, Dejerine, Liepmann, Franceschi, Pick's case No. 2), the only atrophied convolutions were exclusively, or generally, the gyri temporales 1 and 2. On the other hand, motor-aphasic symptoms were associated with sensory-aphasic disturbances (my cases 1 and 2, Pick's case 1, Edlich), atrophy also attacked the pars opercularis of $F^3$, together with the other convolutions of the prefrontal lobe. Nor should it be forgotten that in Shaw's case, and in my case 2, in which symptoms of word-blindness were also recorded, the left gyrus angularis was noticeably more atrophied than the other convolutions.

The relation between the cortical zone, which is the seat of the atrophy, and certain special aphasic symptoms ought, however, to be further investigated. It may here be called to mind that, according to some investigators, the fact that amnesic aphasia gradually produces loss of command of words is due to the ever-increasing affection of the temporal convolutions, while others hold that under these circumstances the process is not limited to the temporal lobe, but extends to the other zones of the hemispheres. This is the opinion of Pick; he points out that in the course of senile atrophy of the brain, even where the temporal lobes are also much atrophied, no noticeable loss in the command of words occurs, even if the patient no longer understands what he is

saying. According to Pick, the decrease in the command of words is a sign that $F^3$ is attacked. This idea is confirmed by my case where not only $T^1$ was affected, but the whole of the pars opercularis of $F^3$.

As for the word-deafness, Pick holds that, in his case, it was not a question of want of perception of words, because the atrophy had not begun in $T^1$. Rosenfeld is of the same opinion, since his patient, though he was ill for about eleven years, never lost his power of understanding words (nor did his command of language decrease). Macroscopic investigation showed that the $T^1$ was relatively little affected, and that the atrophy had chiefly attacked $T^1$ and $T^2$, together with the gyrus occipito-temporalis. This opinion is also confirmed by my present case, since the right $T^1$ and $T^2$, especially in the median zone, were much atrophied, together with those on the left side, and the histological alterations of the corresponding cortex were considerable, particularly on the left side, while my patient had almost completely lost the power of understanding the significance of words. This, on the other hand, tends further to confirm the belief of the bilateral nature of the seat of auditory word images.

Opinions are at variance concerning the seat of amnesia verborum. Rosenfeld is inclined to think that the centre for the recollection of names is to be found, on the left, in these three convolutions ($T^1$, $T^2$, gyrus occipito-temporalis), because these were the most affected in his patient. Quensel, on the contrary, holds that a morbid process going on in the gyrus angularis and in part of the gyrus supramarginalis (the so-called "via sensoriale anacentrale") should produce symptoms of amnesic aphasia. This opinion is not shared by Rosenfeld, who could not record any considerable reduction in these cerebral regions of the brain of his patient. Others, in conclusion (Wolff, Dejerine), hold that it is impossible to localize amnesic aphasia, since it forms a part of motor aphasia, and depends upon a diffused morbid process affecting the cerebral cortex. Rosenfeld, however, draws attention to the fact that this opinion cannot be unconditionally accepted, for in his patient's case there was certainly a diffused morbid process, but this extended chiefly to the said three convolutions ($T^1$, $T^2$, gyrus occipito-temporalis). From the data of my present case, it is impossible to come to a conclusion in favour of either view, for while it is true that the three convolutions just mentioned were atrophied, if only partially, nevertheless the left gyrus supramarginalis and angularis, as well as the convolutions of the prefrontal lobe, were also affected to a considerable degree. We could, therefore, only logically

deduce from this, that amnesia verborum is not due to a process diffused throughout the whole cerebral cortex. However, it would be illogical, since sufficient proof is lacking, to state that the rest of the cerebral cortex was sound, only because the volume of all the other convolutions was apparently normal. It will therefore be wise provisionally to look upon the most various zones, of the cerebral hemispheres, at least to some extent, as the anatomical ground of amnesic aphasia (v. Monakow and others).

Amongst the disphasic disturbances which sometimes occur during the course of aphasia due to atrophy of the convolutions, echolalia is mentioned. The seat of this symptom is also very far from determined. There are two kinds of echolalia: the one consists in the repetition, in the form of a question, of that which has been asked, and which has been understood (Pick), and the other in an automatic, forced repetition (echolalia automatica). Now, since the path of speech, by means of which the repetition is effected, is the oldest in ontogeny (as is shown by the development of speech in young children), it is clear why the second kind of echolalia occurs in the case of senile atrophy which is confined to the left temporal lobe, only at a stage when the sense of words is no longer understood (Liepmann) and, in truth, if the stimulation of the sensory centre of speech no longer awakens any response in the other cortical regions, it finds a vent along the more ancient path of speech (motorial path).

It therefore follows that it is impossible for the complete physiological separation of the temporal lobe from the other speech zones to arise from the atrophy of the temporal lobe alone, and it is thus logical to think that other parts of the cerebral cortex are also involved, and, therefore, that forced automatic echolalia represents a very marked degree of sensory transcortical aphasia, and hence is only found in serious degradation of the psychic functions. Accordingly it is not to be wondered at if two of Pick's cases (Ruczica and Pal) in which automatic echolalia occurred, manifested in the highest degree general atrophy of the brain and of the left cerebral hemisphere in particular. In the case of my patient No. 2 also, where atrophy had not only extended to the temporal lobe but also to the frontal lobe, the echolalia had become automatic only three years after the beginning of the illness. In Dejerine's case, on the other hand, where the brain was normal, with the exception of the two temporal lobes, the symptom in question was entirely absent. The same may be said of Liepmann's case, in which there was atrophy of the left temporal lobe alone. Perhaps the

simultaneous atrophy of the right temporal lobe may contribute to automatic echolalia; that hypothesis is favoured by the case of my patient, where the cortex of the right gyrus temporalis supremus also presented histological alterations.

It is thought that the study of cases of partial atrophy of the brain may open the way for the acceptance of the belief in the localization of psychic functions, and therefore that these cases might form the point of departure for a topographical psychology. Unfortunately, the problem is far less simple. Here, it is true, we have a limited loss of large nerve elements which present a functional, and perhaps an anatomical unity. Nevertheless, in these cases, it is not permissible to establish a connexion between clinical symptoms and histological data, both because the intelligence of the patients who present themselves for examination is already so much enfeebled that it is impossible to investigate exactly the psychic symptoms, and because also they are sometimes suffering from word-deafness. Thus in the case of my patient it was impossible to undertake my researches in this direction, and we were obliged to content ourselves with the study of his behaviour and conduct.

The data reported in the preceding pages testify clearly to the importance of the frontal lobes for cupraxia. Thus, Pick noted that one of his patients, who was suffering from serious atrophy of the frontal lobe, experienced difficulty in managing objects in common use. He, however, believes that this motor apraxia (in truth somewhat mixed) depended upon the atrophy being limited to the frontal lobe. In my cases Nos. 1 and 2, in which the atrophy of the gyri præfontales was also very great, the apraxic symptoms had attributes which were entirely those of extreme visual agnosia. At any rate it is not necessary to conclude that the aphasic and asymbolic (apraxic) manifestations are due to dementia, since sometimes, as in Edlich's case, dementia may not have already declared itself clearly at the period when the said symptoms prevailed.

I will remind the reader in this connexion of the phenomena of psychic blindness present in my case No. 2, and also in others. Psychic blindness and amnesic aphasia often proceed *pari passu*. To understand this, it is only necessary to remember that speech is a highly differentiated mental process, which has been acquired late in ontogeny, and is readily affected by any decrease in psychic power. This is shown by the difficulty in speaking experienced on waking, and when suffering from fatigue, or from any shock, although other functions remain intact.

In old age, the difficulty found in recalling words is due to an incapacity of raising the optic stimulus to the point of producing a response in parts which, in their turn, have become difficult to excite. Therefore, in the greater number of cases of pure cortical blindness, we find a certain amount of amnesic aphasia present; this shows that the stimuli conveyed to the visual cortex, and the revival of the conceptual complexes, are no longer sufficiently strong, if the zone of the sensory aphasia begins to atrophy, and that, further, mental visual stimuli will not succeed in evoking them. If, then, both the spheres are affected by incipient atrophy, but one more seriously than the other, as in many of our cases, it is clear why, even from the beginning of the disease, amnesic aphasia is a symptom often associated with visual agnosia. For this reason disturbances, similar to those which accompany psychic blindness, are often found in our cases. Let me remind the reader of the difficulty in recognizing objects, in recalling immediate images and names, the increased slowness of identification, the feeling of disorientation, the want of visual attention, and hence the difficulty of comprehending the whole together with the parts. All these troubles we find present, and a little accentuated, in the beginning of old age (Stauffenberg); and in fact to-day the pathology of the cerebral cortex has taught us that cortical plaques (a cytopathological sign of senility) are to be met with as much in incipient normal old age, as in eyes of old persons affected by conspicuous mental weakness (F. Constantini).

The results of the microscopic investigations of the circumvolutions when compared with the different clinical pictures reported in the foregoing pages, confirm us still more in the belief that the different forms of aphasia dependent upon the atrophy of the gyri are specially due to the degeneration or the disappearance of the nerve elements lying in defined cerebral regions. In fact, the researches have taught us that echolalia only becomes automatic when the atrophy extends beyond the left temporal lobe, whereas if it is confined to this lobe the disturbance consists only of a partial sensory aphasia. Further, symptoms of motor aphasia (reaching the point of dumbness) are associated with the preceding troubles only when $F^2$ and the insula participate in the atrophy, and finally, the wider the atrophy becomes diffused the more clearly do the sensory aphasic disturbances and the signs of dementia manifest themselves. This does not testify completely in favour of the idea that the whole cerebral cortex contributes to the comprehension of the signification of heard verbal symbols (v. Monakow). Certainly, the more difficult it is to evoke a representative image in consequence of

the extension of the atrophy over the various regions of the cortex, the more marked will be the difficulty in recalling words, and if the processes of mental synthesis become difficult owing to the same pathological cause, the comprehension of what is read, or heard, also is attended with greater trouble.

It would be very daring to deduce from such a small number of cases, some of which have been reported in a summary manner, criteria for determining during life whether a certain aphasic syndrome is due to progressive atrophy of the cerebral convolutions, or whether it depends upon a destructive focus situated in the speech region. But, in any case, a few considerations may be of some use in enabling us to proceed to a differential diagnosis. Points in favour of a cortical, or subcortical, focus of destruction are the sudden manifestation of the aphasia, or at any rate the existence of transitory prodromal symptoms only. On the other hand, in cases of aphasia due to atrophy of the convolutions, a stroke is nearly always absent, the speech troubles begin and increase with excessive slowness, so that it is difficult, even approximately, to determine the time of the appearance of the first symptoms. Nevertheless, sometimes, as in the case of Shaw's patient and of my No. 2, the first speech troubles were recorded as occurring immediately after a species of stroke, which was followed by transitory paresis of the limbs. A second criterion for differentiating between the various kinds of aphasia is the simultaneous presence of severe paralysis of the limbs, since facio-linguo-brachial monopareses (or monoplegias) are often associated with aphasia due to the destruction of the speech zone, especially in motor aphasia, or hemiparesis of the right side, which is sometimes flaccid and sometimes spastic, according to the extension, the seat, or the date of the beginning of the lesion. Motor troubles of such severity are never observed in cases due to atrophy of the convolutions. However, the presence of slight paresis of one side is not irreconcilable with the disease in question; it is only sufficient to call to mind my No. 2, in which the muscular strength of the right side was weaker than that of the left, and in which there also was present paresis of the right half of the tongue. Frequently also, in aphasia following the atrophy of convolutions, the action of the tendon reflexes is on both sides; this does not occur in aphasia due to the focal lesions. It may, however, happen that the Achilles reflexes are exaggerated on one side, even to the point of foot clonus (my case No. 2).

Hence, it follows that in some cases, and especially when a clinical history is absent, which could furnish us with precise data

as to the manner in which the aphasic troubles have developed, it will not be easy to give an opinion on the pathogenesis of the aphasic symptoms. In the present case, indeed, I succeeded in forming a correct judgment during life, basing my conclusions upon the fact that the sensory amnesic and aphasic troubles had developed slowly, that notable disturbances in the motor power, of the limbs at least, were wholly absent, and finally, that the patellar and the superior tendon reflexes were equal on both sides.

Sometimes it may be doubtful, especially where symptoms of word-deafness are dominant, whether the incapacity to understand the meaning of any question whatever is a sign of simple senile dementia. Nevertheless, analysis of the symptoms will always form some basis from which to arrive at a correct decision. Thus, for example, even in the most advanced stages of this psychosis, the patients always understand a certain number of questions, and do not reply like an echo, much less do they lose all command of language to such an extent as scarcely to be able to use one or two words. On the other hand, even in the total wreck of the intellect, such as occurs in advanced senile dementia, loss of the memory of graphic symbols has never been observed.

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# A STUDY OF THE SATELLITE CELLS IN FIFTY SELECTED CASES OF MENTAL DISEASE.

BY SAMUEL T. ORTON, M.D.

*(From the Laboratory of the Worcester State Hospital, Massachusetts.)*

In the normal cerebral cortex, both human and animal, there are found at the base of many of the large pyramidal cells one or two small cells lying between the basal processes and, as a rule, in close association with the point of origin of the axis-cylinder.

There has been some question as to whether these cells should be regarded as neuroglial in origin, or cells of the lymphocytic series. By the ordinary staining methods their morphology is very similar to that of the lymphocyte, except that the nucleus is often less deeply stained and bears a more loosely woven chromatin mesh, while some even appear vesicular. On the other hand it is rare, even among the vesicular forms, to find a nucleus which is oval, or as large as the ordinary glia cell. The lymphocyte is not as a rule an active phagocyte, while the satellite seems prone to take on neurophagocytic activity. In conditions associated with marked perivascular extravasation, such as general paralysis and chronic meningitis, the lymphocytes are closely packed in the perivascular spaces, but do not apparently tend to penetrate the surrounding nervous tissues. Many such cases show, it is true, a more or less active satellitosis, but this reaction is almost without exception in the deeper cell lamina, while the perivascular accumulations are diffuse, or even more intense in the superficial layers.

Cajal accepts the neuroglial origin of these cells and speaks of them as basal neuroglia cells. He calls attention to the fact that they are in relation with that part of the cone of origin and early course of the neuraxon which is not covered with myelin, and suggests that they may serve to insulate these structures from surrounding non-medullated fibres. In the cerebellum of the rabbit, he has described a cell which he classes as a displaced stellate cell of Golgi.* In the cerebellum of the majority of animals those cells are found in the granule layer and give off non-medullated axons which arborize in the granule layer. The

displaced cells in the rabbit lie in the plexiform zone and their axons would thus be exposed to contact with other bare fibres of this layer. Cajal states that these cells may be recognized not only by their morphology but by the mass of accompanying nuclei of the neuroglia type which surround the axon and base of the cell, and here again suggests an insulating capacity for the satellite.

In pathological conditions the satellite becomes of greater interest. Especially is this true of the acute degenerative conditions which have been studied by Alzheimer in great detail by the aid of special staining methods. These include the toxic and infective deliriums and the experimental toxic states, as well as the severe acute manifestations of such diseases as katatonia, status epilepticus and the acute delirious type of general paralysis. In these conditions the cells at the bases of the pyramids are increased in number and show, with appropriate staining methods, a large protoplasmic body which may take on amœboid forms, may contain lipoid, or fuchsinophile, or other granules, and may be actively neurophagic. Alzheimer's work leaves little doubt that these reactive cells are of glial origin, but of a type not active in the production of fibres.

Another change in the normal relation of these cells is that of increase of number without the variety of alterations observable in the acute processes. This is the condition spoken of as satellitosis, and its occurrence has been noted in a number of diseases. As a rule the increase is most noticeable in the deeper cell laminæ of the cortex, and it is rather the exception to see any considerable number of them above the stellate layer.

The fifty cases forming the basis of the present study were selected to form five groups of ten each. These are: Maniacal depressive insanity, dementia præcox, senile dementia, general paralysis and alcoholic insanity. All three types are included among the dementia præcox cases, while the cases of the senile dementia group have been selected to exclude those showing gross brain disease, but not those showing moderate cerebral atrophy or arteriosclerosis.

With few exceptions the counts have been made from material fixed in alcohol, embedded in paraffin, cut at 10 $\mu$ and stained with Nissl's soapy methylene blue. The exceptions are from cases in which the brain was fixed in toto in formalin. This material was also cut into sections by the paraffin method at 10 $\mu$ and stained in thionin, so that the results should be comparable within reasonable limits of error. In all cases five areas from the neopallium were examined. The sites of the sections were as follows:—

Precentral or motor cortex (PCl.): Block taken from about the mid-portion of the ascending frontal or precentral gyrus in approximately the arm area.

Postcentral cortex (PoCl): Block taken from the ascending parietal or postcentral gyrus opposite the precentral block.

Frontal cortex (F.): Block from the first frontal gyrus along the margin of the great longitudinal fissure about midway between the frontal pole and the Rolandic fissure. In some of the cases this block yields sections showing a stellate layer and hence belongs in the true frontal type of cortex (Campbell's classification). Some showed no definite stellate layer (indicated in the tables by an absence of figure in lamina 4) and hence probably belong in the intermediate precentral field.

Temporal cortex (T.): Block from the first temporal gyrus, lateral surface along the lip of the fissure of Sylvius about midway between the line of projection of the anterior sylvian trunk and the point of division of the posterior or main sylvian fissure and hence representing auditopsychic cortex.

Occipital cortex (Occ.): This material is not constant in origin. Some sections are of calcarine or visuosensory cortex and some are of the common occipital or visuopsychic field. The sections from the calcarine area may be identified in the charts by the absence of a figure in the lamina ganglionaris, as no attempt was made to count the satellites in this layer as will be explained below.

The count has been made to include the two major points of interest, viz.: The number of satellites and their distribution by laminæ. Brodmann's division of the neopallial cortex into six layers—i.e., (1) zonalis, (2) granularis externa, (3) pyramidalis, (4) granularis interna, (5) ganglionaris, and (6) multiformis—has been adopted for this purpose, and an attempt has been made to count only cells which conform to the type of each layer. Thus in the lamina pyramidalis only large pyramidal cells have been counted, &c. This leads to some difficulty in some cortices, such as the precentral and agranular frontal which are without a well-developed lamina granularis interna and in the calcarine where the granule layer is reduplicated and the lamina pyramidalis is not well supplied with characteristic cells homologous to those in other regions. It has seemed advisable, however, for the present purpose to use one classification for all cortices, and hence the counts are made with the omission of a figure in lamina 4 of the precentral and agranular frontal, and in lamina 5 of the calcarine, while

the reduplicated lamina granularis interna of the visual cortex has been considered as one layer. No effort was made to estimate the numbers of neuroglia nuclei in the zonal layer.

In each lamina the count has been made by recording the number of satellites found in association with 20 representative cells and record is made in increments of 10. Thus the association of 20 or less satellites with 20 nerve-cells has been considered negative; from 21 to 30 satellites with 20 nerve-cells is considered as a ratio of 1·5 to 1; 31 to 40 satellites, to 20 nerve-cells, as of 2 to 1, &c. Only those cells in immediate relation with a nerve-cell have been counted, and no cognizance is taken of the clusters of neuroglia nuclei about vessels, nor in spaces in the fibre layers which may have originally contained nerve-cells.

## RECORD OF COUNTS.

### I.—Maniacal Depressive Group.

*Case* 1.—Maniacal depressive insanity: maniacal form. Third attack: eleven years' duration.[1] Age at death, 65 years. Autopsy number, xv-15.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 0 | 1—1 |
| (5) | 1·5—1 | 1—1 | 1·5—1 | 1·5—1 | — |
| (6) | 1·5—1 | 1·5—1 | 2—1 | 2—1 | 1·5—1 |

*Case* 2.—Maniacal depressive insanity: depressed form. Third attack: duration twenty-seven years. Age at death, 68 years. Autopsy number, xvi-34.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 0 | 0 |
| (4) | — | 1—1 | | 0 | 0 |
| (5) | 1—1 | 1·5—1 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 3.—Maniacal depressive insanity: depressed form. Three years' duration. Age at death, 61 years. Autopsy number, xvi-42.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 1—1 | 0 |
| (4) | — | 1—1 | 1—1 | 1—1 | 1—1 |
| (5) | 1—1 | 1·5—1 | 1—1 | 1—1 | 1—1 |
| (6) | 1—1 | 2—1 | 2—1 | 1·5—1 | 1—1 |

[1] In the maniacal depressive series the duration is given as from the time of onset of the first attack.

*Case* 4.—Maniacal depressive insanity: circular form. Multiple attacks: duration, forty-five years. Age at death, 74 years. Autopsy number, xvii-10.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1–1 | 0 | 1–1 | 1–1 | 0 |
| (4) | — | 1–1 | 1–1 | 1–1 | 1–1 |
| (5) | 1–1 | 1–1 | 1·5–1 | 1·5–1 | — |
| (6) | 1·5–1 | 1·5–1 | 1·5–1 | 2–1 | 1–1 |

*Case* 5.—Maniacal depressive insanity: maniacal form. First attack: duration, five and a half years. Age at death, 35 years. Autopsy number, xvii-17.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1–1 | — | 0 | 0 |
| (5) | 1–1 | 1–1 | 1–1 | 1–1 | — |
| (6) | 1·5–1 | 1·5–1 | 1·5–1 | 1–1 | 1·5–1 |

*Case* 6.—Maniacal depressive insanity; maniacal form. First attack; duration, two months. Age at death, 41 years. Autopsy number, xvii-32.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 1–1 | 1–1 | 1–1 | 0 | 0 |
| (6) | 1–1 | 1–1 | 1·5–1 | 1–1 | 1–1 |

*Case* 7.—Maniacal depressive insanity: maniacal form. Sixth attack; duration, thirty-one years. Age at death, 66 years. Autopsy number, xvii-48.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 1–1 | 0 | 0 |
| (4) | — | 1–1 | 1–1 | 0 | 1–1 |
| (5) | 1–1 | 1–1 | 1–1 | 1–1 | — |
| (6) | 1–1 | 1–1 | 1·5–1 | 1–1 | 1–1 |

*Case* 8.—Maniacal depressive insanity; depressed form. First attack; duration, five years. Age at death, 41 years. Autopsy number, xvii-49.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1–1 | — | 0 | 1–1 |
| (5) | 1–1 | 1–1 | 1–1 | 1–1 | 1–1 |
| (6) | 1–1 | 1–1 | 1·5–1 | 1–1 | 1·5–1 |

*Case* 9.—Maniacal depressive insanity: maniacal form. Third attack; duration, seventeen years. Age at death, 70 years. Autopsy number, xvii-59.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 1—1 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 1·5—1 | 1—1 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 1—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 10.—Maniacal depressive insanity: maniacal form (some depressions). Eleventh attack; duration, thirty-one years. Age at death, 75 years. Autopsy number, xiii-12.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 0 | 0 | 0 |
| (4) | — | 1—1 | — | 1—1 | 1—1 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |
| (6) | 1·5—1 | 1·5—1 | 1—1 | 1·5—1 | 1·5—1 |

## II.—Dementia Præcox Group.

*Case* 1.—Hallucinatory type; slight deterioration. Duration, eight months. Age at death, 31 years. Autopsy number, xv-22.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | 0 |
| (6) | 1·5—1 | 1·5—1 | 0 | 0 | 0 |

*Case* 2.—Dementia præcox: hebephrenic form. Duration, three years. Age at death, 45 years. Autopsy number, xv-58.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | — |
| (6) | 0 | 0 | 0 | 0 | 0 |

*Case* 3.—Dementia præcox: paranoid form. Duration, seven years. Age at death, 52 years. Autopsy number, xv-58.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | — |
| (6) | 0 | 0 | 0 | 0 | 0 |

*Case* 4.—Dementia præcox: paranoid form. Duration, thirty-one years. Age at death, 69 years. Autopsy number xv-67.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 1—1 | 0 | 0 |
| (5) | 1—1 | 1—1 | 0 | 0 | — |
| (6) | 1—1 | 1—1 | 2—1 | 1—1 | 1—1 |

*Case* 5.—Dementia præcox: katatonic form. Duration, three years. Age at death, 41 years. Autopsy number, xv-79.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | — |
| (6) | 0 | 0 | 0 | 0 | 0 |

*Case* 6.—Dementia præcox: paranoid form. Duration, thirteen years. Age at death, 43 years. Autopsy number, xv-84.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | — |
| (6) | 0 | 0 | 0 | 0 | 0 |

*Case* 7.—Dementia præcox: hebephrenic form. Duration, seven years. Age at death, 29 years. Autopsy number, xvi-37.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | — |
| (6) | 0 | 1—1 | 1—1 | 1·5—1 | 0 |

*Case* 8.—Dementia præcox: paranoid form. Duration, forty-six years. Age at death, 83 years. Autopsy number, xvii-4.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 1—1 | 1—1 |
| (4) | — | 0 | 0 | 1—1 | 1—1 |
| (5) | 1—1 | 1—1 | 1—1 | 1·5—1 | — |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1·5—1 |

*Case* 9.—Dementia præcox; hebephrenic form. Duration, twenty-eight years. Age at death, 63 years. Autopsy number, xvii-14.

| | PCL | PoCL | F | T | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | 0 |
| (6) | 1—1 | 1—1 | 1—1 | 1—1 | 1·5—1 |

*Case* 10.—Dementia præcox: katatonic form. Duration, twenty-five years. Age at death, 60 years. Autopsy number, xvii-16.

| | PCL | PoCL | F | T | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | 0 |
| (6) | 0 | 0 | 1·5—1 | 1—1 | 1—1 |

## III.—Senile Group.

*Case* 1.—Senile dementia. Duration, six months. Age at death, 74 years. Autopsy number, xv-17.

| | PCL | PoCL | F | T | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1—1 | 0 | 0 | 0 |
| (5) | 1·5—1 | 1—1 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 1·5—1 | 2—1 | 1·5—1 | 1—1 |

*Case* 2.—Senile dementia. Duration, nine years. Age at death, 73 years. Autopsy number, xv-18.

| | PCL | PoCL | F | T | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 1—1 | 0 | 1—1 |
| (4) | — | 0 | 1—1 | 0 | 1—1 |
| (5) | 1—1 | 1—1 | 1·5—1 | 1—1 | — |
| (6) | 1·5—1 | 1·5—1 | 2—1 | 1—1 | 1·5—1 |

*Case* 3.—Senile dementia. Duration, nine months. Age at death, 75 years. Autopsy number, xv-20.

| | PCL | PoCL | F | T | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 1—1 | 0 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |
| (6) | 1—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 4.—Senile dementia. Duration, one month. Age at death, 75 years. Autopsy number, xv-25.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |
| (4) | — | 1—1 | 1—1 | 1—1 | 1—1 |
| (5) | 1·5—1 | 1—1 | 1—1 | 1·5—1 | 1·5—1 |
| (6) | 2—1 | 1·5—1 | 2—1 | 2—1 | 2—1 |

*Case* 5.—Senile dementia. Duration, five months. Age at death, 76 years. Autopsy number, xv-29.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | |
| (5) | 0 | 0 | 0 | 1—1 | 0 |
| (6) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |

*Case* 6.—Senile paranoid condition. Duration, twenty-five years. Age at death, 83 years. Autopsy number, xv-40.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 0 | 0 |
| (4) | — | 1—1 | 0 | 0 | 0 |
| (5) | 1—1 | 1—1 | 1—1 | 0 | 0 |
| (6) | 1·5—1 | 1—1 | 1—1 | 1—1 | 1—1 |

*Case* 7.—Senile paranoid condition, with dementia. Duration, ten years. Age at death, 78 years. Autopsy number, xv-42.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 0 | 1—1 |
| (5) | 1—1 | 1·5—1 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 8.—Senile paranoid condition. Duration, two years and a half. Age at death, 67 years. Autopsy number, xv-43.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 0 | |
| (4) | — | 1—1 | 1—1 | 0 | 0 |
| (5) | 1·5—1 | 1—1 | 1—1 | 1—1 | — |
| (6) | 2—1 | 1—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 9.—Senile dementia. Duration, one month. Age at death, 62 years. Autopsy number, xv-57.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 1—1 | 0 | 1—1 | 0 | 0 |
| (6) | 1—1 | 1—1 | 1—1 | 0 | 0 |

*Case* 10.—Senile dementia. Duration, nine years. Age at death, 84 years. Autopsy number, xvi-2.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | 0 |
| (6) | 1—1 | 1—1 | 0 | 1—1 | 0 |

## IV.—General Paralysis Group.

*Case* 1.—General paralysis: demented. One year's duration (?). Age at death, 37 years. Autopsy number, xv-24.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 1—1 | 0 | 0 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 2—1 | 1·5—1 | 2—1 | 1—1 |

*Case* 2.—General paralysis: demented. Three years' duration. Age at death, 63 years. Autopsy number, xv-51.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | * | * | * | * | 0 |
| (3) | * | * | * | * | 0 |
| (4) | — | * | * | * | 1—1 |
| (5) | 1·5—1 | * | 1—1 | 1—1 | — |
| (6) | 2—1 | 2—1 | 1·5—1 | 1·5—1 | 1—1 |

* Marked stratigraphic disturbance due to the lesions of general paralysis.

*Case* 3.—General paralysis. Four years' duration. Age at death, 43 years. Autopsy number, xv-33.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 0 | 0 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 | 1—1 |

*Case* 4.—General paralysis. Two years' duration. Age at death, 42 years. Autopsy number, xv-34.

| | PCl. | PsCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | * | * | 0 | 0 |
| (4) | — | * | * | 0 | 0 |
| (5) | 1—1 | * | * | 1—1 | — |
| (6) | 1·5—1 | 2—1 | 1·5—1 | 1—1 | 1—1 |

* Marked stratigraphic disturbance due to the lesions of general paralysis.

*Case* 5.—General paralysis. Two years' duration. Age at death, 54 years. Autopsy number, xv-41.

| | PCl. | PsCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 0 | 0 |
| (5) | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 | 1—1 |
| (6) | 2—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 6.—General paralysis. One and a half years' duration. Age at death, 55 years. Autopsy number, xv-47.

| | PCl. | PsCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 0 | 0 |
| (4) | — | 1—1 | — | 0 | 1—1 |
| (5) | 1—1 | 0 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 | 1—1 |

*Case* 7.—General paralysis. Six months' duration (?). Age at death, 36 years. Autopsy number, xvi-9.

| | PCl. | PsCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | 0 |
| (6) | 1·5—1 | 1—1 | 1·5—1 | 1—1 | 1—1 |

*Case* 8.—General paralysis. One year's duration. Age at death, 60 years. Autopsy number, xvi-14.

| | PCl. | PsCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 1—1 | 1—1 | 0 | 0 | 0 |
| (6) | 1·5—1 | 1—1 | 1—1 | 0 | 0 |

*Case* 9.—General paralysis. Seven years' duration. Age at death, 49 years. Autopsy number, xvi-15.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 0 | 0 |
| (5) | 1—1 | 1—1 | 1·5—1 | 1—1 | 0 |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1·5—1 | 0 |

*Case* 10.—General paralysis. Two years' duration. Age at death, 40 years. Autopsy number, xvi-26.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 0 | 0 | 0 |
| (4) | — | 1—1 | 1—1 | 0 | 0 |
| (5) | 1·5—1 | 1·5—1 | 1—1 | 1—1 | 0 |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 | 0 |

## V.—Alcoholic Insanity Group.

*Case* 1.—Alcoholic deterioration. Duration, three years.[1] Age at death, 46 years. Autopsy number, xv-44.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | — |
| (6) | 1—1 | 1—1 | 1—1 | 0 | 0 |

*Case* 2.—Alcoholic deterioration. Duration, five years. Age at death, 61 years. Autopsy number, xv-45.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 1—1 | 1—1 | 0 | 0 | 0 |
| (6) | 1—1 | 1—1 | 1—1 | 0 | 0 |

*Case* 3.—Alcoholic paranoid condition. Duration, nine years. Age at death, 37 years. Autopsy number, xv-73.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | — |
| (6) | 1·5—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 |

[1] In the alcoholic group duration refers to duration of the psychosis, not the habit.

*Case* 4.—Alcoholic deterioration. Duration, sixteen years. Age at death, 58 years. Autopsy number, xvi-16.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 0 | 0 | 0 | 0 |
| (5) | 0 | 0 | 0 | 0 | 1—1 |
| (6) | 0 | 0 | 1—1 | 0 | 1—1 |

*Case* 5.—Alcoholic paranoid condition. Duration, one month. Age at death, 61 years. Autopsy number, xvi-19.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 0 | 1—1 | 0 | 0 |
| (4) | — | 1—1 | — | 0 | 0 |
| (5) | 1·5—1 | 1—1 | 1·5—1 | 1—1 | 1—1 |
| (6) | 2—1 | 1—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 6.—Alcoholic deterioration. Duration, one month. Age at death, 65 years. Autopsy number, xvi-32.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 1—1 | 0 |
| (4) | — | 1—1 | — | 1—1 | 1—1 |
| (5) | 1·5—1 | 1·5—1 | 1—1 | 1—1 | — |
| (6) | 2—1 | 1·5—1 | 1·5—1 | 1·5—1 | 1—1 |

*Case* 7.—Alcoholic deterioration. Duration, six months. Age at death, 68 years. Autopsy number, xvii-13.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |
| (4) | — | 1—1 | 1—1 | 1—1 | 1—1 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | 1—1 |
| (6) | 1·5—1 | 1·5—1 | 1—1 | 1·5—1 | 1·5—1 |

*Case* 8.—Korsakow psychosis. Duration, ten years. Age at death, 57 years. Autopsy number, xvii-28.

| | PCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1—1 | — | 0 | 0 |
| (5) | 1—1 | 1—1 | 1—1 | 1—1 | 0 |
| (6) | 1—1 | 1—1 | 1·5—1 | 1·1 | 1—1 |

*Case* 9.—Delirium tremens. Duration, several days. Age at death, 42 years. Autopsy number, xvii-33.

| | PrCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 0 | 0 | 0 | 0 | 0 |
| (4) | — | 1–1 | — | 0 | 0 |
| (5) | 1–1 | 1–1 | 1–1 | 1–1 | 0 |
| (6) | 1–1 | 1·5–1 | 1·5–1 | 1–1 | 1–1 |

*Case* 10.—Alcoholic deterioration. Duration, two years. Age at death, 61 years. Autopsy number, xvii-38.

| | PrCl. | PoCl. | F. | T. | Occ. |
|---|---|---|---|---|---|
| (1) | — | — | — | — | — |
| (2) | 0 | 0 | 0 | 0 | 0 |
| (3) | 1–1 | 1–1 | 0 | 0 | 0 |
| (4) | — | 0 | — | 0 | 0 |
| (5) | 1–1 | 1–1 | 1–1 | 1–1 | 0 |
| (6) | 1·5–1 | 1–1 | 1–1 | 1–1 | 1–1 |

## Analysis and Discussion.

In order to enable the more ready interpretation of the foregoing data in analytical form it has been deemed advisable to reduce the tables to a figure which will indicate at once the relative severity of reaction both in regard to the number of laminæ involved and the grade of involvement in each. This figure, which for convenience will be called the satellite index, is made up by counting the number of layers involved, giving each at the same time a value equivalent to the satellite—nerve-cell ratio. Thus the post-central cortex of Case I. 1, shows three laminæ with a count of 1 to 1 and one of 1·5 to 1, giving a satellite index of 4·5 while the frontal cortex of the same case has two laminæ with 1 to 1 reaction, and one each of 1·5 to 1 and 2 to 1, giving an index of 5·5. In all cases where a layer is wanting, e.g., precentral stellate the interpretation has been made on the basis of the layer immediately above. That is the occurrence of a 1 to 1 reaction in the lamina ganglionaris is taken as evidence of an extension of the process above the position which a stellate layer would occupy and is considered as though a similar reaction occurred there. These methods of analysis are of course open to some question, but they will probably indicate the conditions within reasonable limits of error.

The records all tend to show a marked predilection for the deeper cell layers. Almost without exception the numerical record shows slight, if any, reaction in the upper laminæ, but a marked tendency

to an increasing ratio as one after another of the subjacent laminæ is reached. Not only does the reaction tend to increase as one passes to the deeper layers, but even within one layer there may be a noticeable difference at various levels. Thus the deeper portions of the lamina pyramidalis and the lamina multiformis contain a noticeably larger number of satellites in the majority of instances than the upper levels. (This has been taken into account in the record of findings as mentioned above.) No attempt has been made to estimate the number of cells of the neuroglia type in the subcortical white matter, but the survey has given rise to a strong impression that those cases showing marked satellitosis also show an increase here.

An analysis of the satellite indices by laminæ of the whole series gives the following results :—

| Lamina | Total indices (50 cases) | Average index |
|---|---|---|
| Granularis externa (2) | 0 | 0 |
| Pyramidalis (3) | 59 | 1·18 |
| Granularis interna (4) | 88 | 1·76 |
| Ganglionaris (5) | 171·5 | 3·43 |
| Multiformis (6) | 276·5 | 5·53 |

The increase on reaching successively deeper layers is strikingly shown.

There is also a fairly constant tendency toward milder involvement of the occipital and temporal regions, as is shown by the following table :—

| Region | Total indices (50 cases) | Average index |
|---|---|---|
| Precentral | 149·5 | 2·99 |
| Postcentral | 131·5 | 2·63 |
| Frontal[1] | 132·0 | 2·64 |
| Temporal | 102·5 | 2·05 |
| Occipital[2] | 79·5 | 1·59 |

[1] Eighteen of the fifty cases represent a-granular frontal or cortex of the effector type.
[2] Twenty-three of the fifty cases are calcarine cortex.

In this table it must be considered that the inclusion of ten cases of general paralysis in which the severest expression is usually prerolandic or involves the pre-rolandic and post-central fields might play some part, but a similar analysis of the averages with the general paralysis series omitted has yielded about the same result.

The analysis by groups of psychoses has been carried out in a slightly different manner. In order to simplify the interpretation the cases have been separated into five groups, viz., (1) negative, those with a satellite count less than the nerve-cell count in all laminæ; (2) slight, where the satellite index was below 5; (3) moderate, with

a satellite index between 5·5 and 10; (4) marked between 10·5 and 15; and (5) intense with an index above 15·5. This arrangement has yielded the following result:—

| | Negative | Slight | Moderate | Marked | Intense |
|---|---|---|---|---|---|
| Maniacal depressive | 0 | 0 | 1 | 4 | 5 |
| Dementia præcox | 4 | 4 | 2 | 0 | 1 |
| Senile psychoses | 0 | 2 | 1 | 4 | 3 |
| General paralysis | 0 | 0 | 2 | 6 | 2 |
| Alcoholic psychoses | 0 | 3 | 0 | 4 | 3 |

The most striking results of this analysis are the relation of the maniacal depressive and dementia præcox groups.

The first group, that of the maniacal depressive series, shows a marked tendency towards high indices, with one case in the moderate column and all of the remainder either marked or intense, while the dementia præcox group, in sharp contrast, shows fairly consistent low indices. This condition in dementia præcox stands in sharp contrast to the active neuroglia reaction (amœboid neuroglia and neurophagocytosis), which Alzheimer and others have shown in the active stages of the disease, but these changes are probably evanescent and would not be expected to play an important rôle in a series of cases such as the present, which are for the most part of long standing. Alzheimer emphasizes that the degree of these changes is in relation to the severity of the attack rather than its clinical expression, and that soon after an acute catatonic "storm," for instance, little of this sort of alteration may be demonstrable. In none of the other three groups were there cases of entirely negative count, but otherwise the distribution is more general.

In the one case of moderate reaction of the maniacal depressive group (Case I, 6) the patient died at the age of 41, while the patient with dementia præcox with an intense reaction lived to be 83. To control the influence of age the data have been arranged in a table by decades with the following result:—

| | Negative | Slight | Moderate | Marked | Intense |
|---|---|---|---|---|---|
| Under 30 | 0 | 1 | 0 | 0 | 0 |
| 31–40 | 0 | 1 | 1 | 5 | 0 |
| 41–50 | 3 | 1 | 1 | 3 | 1 |
| 51–60 | 1 | 2 | 1 | 2 | 1 |
| 61–70 | 0 | 2 | 2 | 5 | 6 |
| 71–80 | 0 | 0 | 1 | 2 | 5 |
| Over 81 | 0 | 1 | 0 | 1 | 1 |

This table seems to indicate a tendency for the more intense reactions to occur in the latter decades, but that age is not the only

factor may be seen from Case III, 10, a senile dement, aged 84, with a satellite index of 3, which places it in the slight group.

Finally, the data have been rearranged to determine any possible relation between the duration of the psychosis and the degree of reaction. This is manifestly a difficult task as the time of onset in many of the included cases is difficult to determine with accuracy. In the maniacal depressive group the duration has been reckoned from the onset of the first attack. In the alcoholics no attempt was made to estimate the period of the habit, but the figures are taken from the onset of mental symptoms sufficient to result in hospital commitment. The table follows :—

| | Negative | Slight | Moderate | Marked | Intense |
|---|---|---|---|---|---|
| Less than 1 year | 0 | 2 | 3 | 3 | 1 |
| 1 to 5 years | 2 | 1 | 1 | 8 | 2 |
| 5 to 10 years | 1 | 3 | 0 | 4 | 3 |
| Over 10 years | 1 | 2 | 2 | 3 | 5 |

Here there seems to be no definite relationship. The marked and intense cases are distributed with relative evenness throughout the varying periods. The eight cases in the 1- to 5-year period in the marked column seems disproportionate, but this is accounted for by the occurrence here of six cases of general paralysis.

## Conclusions.

The analysis of the relative numerical occurrence of satellite cells in ten cases, each of five psychoses, seem to warrant the conclusion that satellitosis cannot be considered in any sense indicative of the type of psychosis, although it has in this series appeared with more consistent intensity in the maniacal depressive cases and has been of very much less prominence in dementia præcox.

The reaction elects the deeper cell layers both in regard to frequence of occurrence and degree of reaction.

The cortices of the dome, precentral, postcentral and frontal, seem to show the reaction with greater intensity than do the temporal and occipital regions.

Age at the time of death seems to play some part in the occurrence of severe reactions, but cannot be considered the only factor.

The duration of the psychosis bears no demonstrable relation to satellitosis.

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## Publications Recently Received.

[*Notes on a Book under this heading do not preclude a subsequent review.*]

*Die agrammatischen Sprachstörungen. Studien zur psychologischen Grundlegung der Aphasielehre.* Von Professor Dr. Arnold Pick. Theil i. S. 291. Berlin: Springer, 1913.

The genius of Hughlings-Jackson was of the sort which comes to fruition through the minds of others: those who have been subject to its influence become dissatisfied with the idols of the market-place. The author of this monograph, of which the first part only has so far appeared, is probably the profoundest living student of Hughlings-Jackson's ideas, and his work is a plea for a more modern treatment of the question of Aphasia. For, although psychology is advancing rapidly, these disturbances of speech are still treated as a matter of cerebral "localization"; we hear of "memory pictures deposited in cells" and similar meaningless fantasies. Interest is centred, not on the nature of the disturbance of speech in any particular patient, but on the "localization" of the cause, which is supposed to underlie its appearance. Consequently we know something of the gross anatomy and diagrammatic symptomatology of certain brain lesions, but nothing about the real nature of defects of speech. This book begins with a plea for clear thinking, and a clean slate. The doctrines of aphasia are crusted with obsolete psychology and false physiology. The author passes on to consider the nature of a sentence, how it is built up, and in how far it exhibits the "propositioning function." He deals with the means of expression in speech, the way from thought to expression, Wundt's "Gesammtvorstellung" and the question of internal speech. This is one of the most stimulating books in neurology we have come across for a long time, and should serve to sweep away those mists which obscure the coming of a more modern doctrine of the higher disturbances of speech. We shall await the appearance of the second part with the greatest interest, and trust it will be furnished with a complete index.

*Sémiologie des Affections du Système Nerveux.* Par J. Dejerine, Professeur de Clinique des Maladies du Système Nerveux à la Faculté de Médecine de Paris. Pp. 1212, avec 560 figures et 3 planches. Paris: Masson, 1914.

More than ten years ago Dejerine wrote a "Sémiologie des affections du système nerveux" for Bouchard's "Traité de Pathologie générale," and the present work is called a Second Edition. But, as a matter of fact, it has been

entirely re-written and brought up to date in a remarkable manner; we know of no account of the symptomatology of nervous disease which contains so many of the more recent additions to knowledge. The book is admirably arranged, clear and lucid in exposition and filled with many new and excellent diagrams. The relation between the complicated anatomy of the brain-stem and the symptoms produced by lesions at various points between the upper end of the spinal cord and the optic thalamus is particularly clearly exposed. Even those to whom the French language is not familiar should possess this book for the sake of its figures alone.

*The Modern Treatment of Nervous and Mental Diseases.* Edited by William A. White, M.D., and Smith Ely Jelliffe, M.D., 2 vols. Illustrated. Pp. 867 and 816. London: Kimpton, 1913.

The first volume of this interesting work is devoted to mental diseases and to the psychical aspect of affections of the nervous system. Each of the nineteen chapters has been handed over to an authority on the subject, and they are all eminently readable. We might, perhaps, single out the chapters on the Educational Treatment of the Feeble-minded (Dr. Goddard), on Immigration and the Mixture of Races (Dr. Salmon), on the Neuroses and Psychoneuroses (Dr. Ernest Jones), and on Maniacal Depressive Insanity (Dr. Farrar).

The second volume is of even greater interest to the neurologist. Mr. Sherren deals with the treatment of injuries of the peripheral nerves; Dr. Jelliffe has written a concise account of headaches and of the treatment of syphilitic diseases of the nervous system. A chapter on Aphasia and Apraxia has been contributed by Dr. S. A. K. Wilson, and Dr. Gordon Holmes deals with the optic thalamus, mid-brain and cerebellum. Surgery of the brain and spinal cord is in the hands of Dr. Halstead and Dr. Vaughan. Many of the chapters have excellent bibliographies and there is a good index.

*Organic and Functional Nervous Diseases.* By M. Allen Starr, M.D., &c. Fourth edition, thoroughly revised. Pp. 970, illustrated with 323 engravings in the text and 30 plates in colours and monochrome. New York and Philadelphia: Lea and Febiger, 1913.

This well-known text-book of nervous diseases has been revised and a good deal of new matter has been added, especially in those parts which deal with the psychoneuroses. But knowledge has advanced so rapidly in the last ten years that no simple revision can be adequate, however excellent a text-book may have been when first published. The effects produced by lesions of the cerebellum, brain-stem, optic thalamus and basal nuclei are given in a somewhat cursory manner. The description of aphasia and allied conditions and of syphilis of the nervous system and its relation to the Wassermann test will require further revision in the next edition.

*Lehrbuch der Nervenkrankheiten.* Von Professor Dr. H. Oppenheim. Sechste, wesentlich vermehrte und verbesserte Auflage. S. 1926, mit 523 Abbildungen im Text und auf 4 Tafeln. Berlin: Karger, 1913.

In essential features the present edition is unaltered. New references have been added and most chapters show additions, especially in the paragraphs in small print dealing with the work of some one observer. The literature has been brought up to date and the number of references to recent papers is remarkable.

*The Psychoneuroses and their Treatment by Psychotherapy.* By Professor Dejerine and Dr. E. Gauckler. Authorized translation by Smith Ely Jelliffe, M.D. Pp. 395. Philadelphia and London: Lippincott, 1913.

This is a translation of the well-known work of Professor Dejerine and his assistant, Dr. Gauckler, which was noticed in Brain, vol. xxxiv, p. 535. The book is of such importance to all who have to deal with the psychoneuroses that we welcome an English translation for those who cannot read it in the original French. Such readers will have to be content with an adequate rendering of its contents, but will miss the enjoyment of the charming style of the original.

*Modern Problems in Psychiatry.* By Ernesto Lugaro. Translated by David Orr, M.D., and R. G. Rows, M.D., with a foreword by Sir T. S. Clouston, M.D. Pp. 305. Manchester: University Press, 1913.

This is an excellent translation of the Second Edition of Professor Lugaro's well-known book. Throughout the standpoint is that of cerebral pathology, and little stress is laid on the part played by psychical processes in mental disease; in fact, this work represents the views of the extreme physical school of alienists. It is well got up and extremely easy to read.

*Psychanalysis.* By A. A. Brill, M.D. Pp. 337. Philadelphia and London: Saunders, 1913.

In this book the psychoneuroses are treated from the strictest Freudian aspect. It forms a clear statement of the views of the Vienna physician on obsessions, hysteria, dreams, the compulsion neuroses, the psychopathology of everyday life and wit, illustrated by many examples.

Writers of "Original Articles and Clinical Cases" are supplied free of charge with 50 copies reprinted in the form in which the paper stands in the pages of "Brain." If reprints are required in pamphlet form, with wrapper, title-page, &c., and re-numbered pages, they must be ordered, at the expense of the writers, from Messrs. BALE, SONS & DANIELSSON, Ltd., 83-91, Great Titchfield Street, London, W.

Members of the Neurological Section of the Royal Society of Medicine can obtain the Index of "Brain" for the Volumes I. to XXIII. inclusive, that is, from its commencement to the end of 1900, from Messrs. MACMILLAN & CO., Ltd., St. Martin's Street, London, W.C., at the price of 6s. 6d., post free.

To those who are not members of the Neurological Section of the Royal Society of Medicine the price is 8s. 6d. net, and the volume may be obtained through any bookseller.

EDITOR.

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